

Supporting Information

Targeting CYP2J for reducing paclitaxel-induced peripheral neuropathic pain

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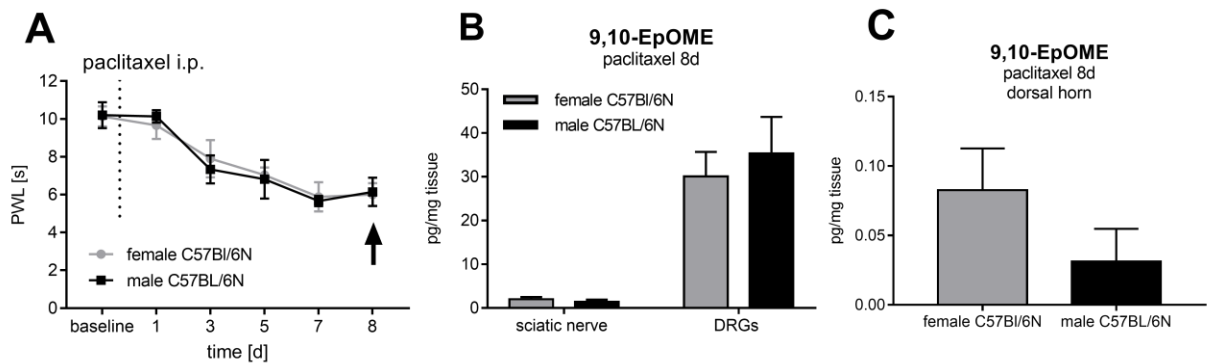


Figure S1: Gender differences in paclitaxel-CIPN and 9,10-EpOME concentrations.

(A) Mechanical thresholds of male (black) vs. female (grey) C57Bl6/N-mice eight days after paclitaxel treatment (6 mg/kg i.p.). At day eight, tissue was dissected (indicated with arrow) and 9,10-EpOME-concentrations were determined via LC-MS/MS. (B) Concentrations of 9,10-EpOME from male (black) vs. female (grey) C57Bl6/N-mice eight days after paclitaxel-injection (6 mg/kg i.p.). Concentrations were determined in sciatic nerve, lumbal DRGs (B) and the dorsal horn of the spinal cord (C). Data are shown as mean \pm SEM from n=6 mice per group.

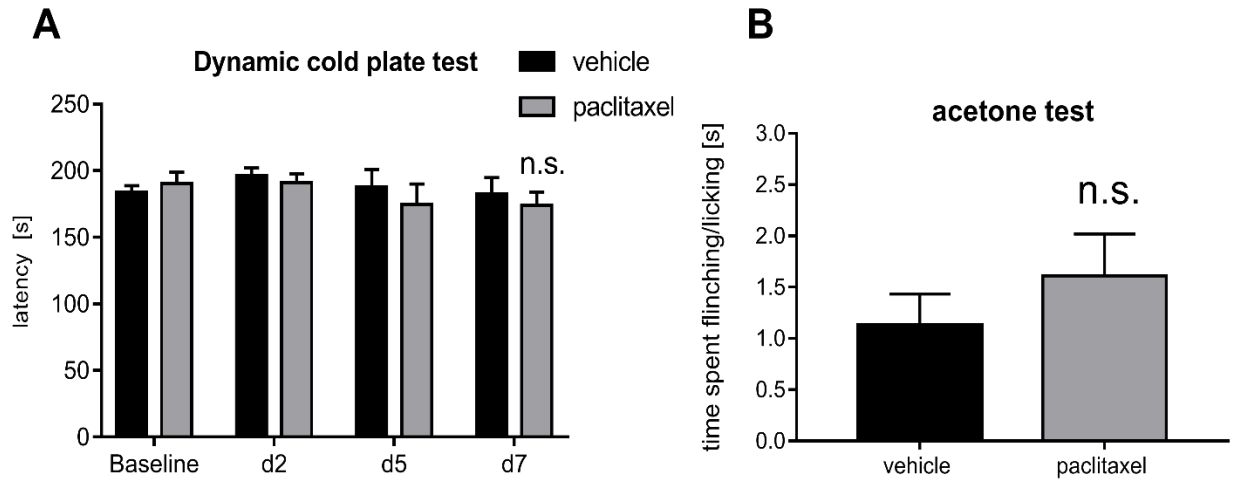


Figure S2: Effects of telmisartan high-dose (6 mg/kg) on cold pain thresholds. (A) Dynamic Cold plate test was performed using a decreasing temperature ramp from 25-0°C at 12°C/min. Cut-off time was set to 200s. Shown are latency times of wild-type C57BL/6N mice receiving vehicle (black bars) or paclitaxel (6 mg/kg i.p., grey bars). Dynamic cold plate test was performed on days 0, 2, 5 and 7 after injection. Data are presented as mean means \pm SEM from n=8 mice per group; n.s.: not significant, two-way ANOVA with Bonferroni's post-hoc test. (B) The acetone test was performed on day 8 after injection of vehicle or paclitaxel (6 mg/kg i.p.). Data are shown as mean means \pm SEM from n=8 mice per group; n.s.: not significant, two-way ANOVA with Bonferroni's post-hoc test.

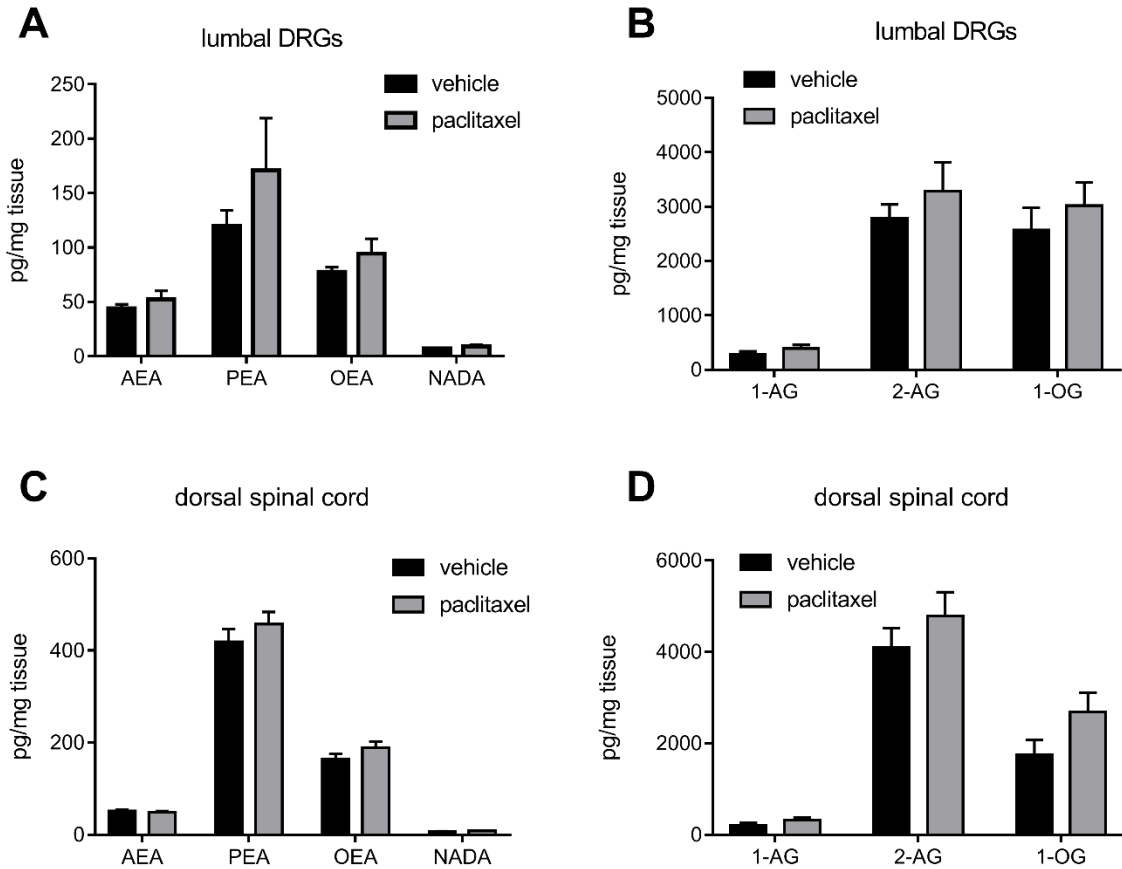


Figure S3: Concentrations of endocannabinoids and endovanilloids eight days after injection of paclitaxel (6 mg/kg i.p.). Concentrations of endocannabinoids anandamide (AEA), palmitoylethanolamide (PEA), oleoylethanolamide (OEA) and the endovanilloid N-arachidonoyl dopamine (NADA) in lumbar DRGs (**A**) or the dorsal spinal cord (**C**) eight days after treatment with vehicle (black) or paclitaxel (grey). Concentrations of the monoacylglycerols 1- and 2-arachidonoylglycerol (1-AG and 2-AG) as well as 1-oleoylglycerol (1-OG) in lumbar DRGs (**B**) or the dorsal spinal cord (**D**) eight days after treatment with vehicle (black) or paclitaxel (grey). Concentrations were determined with LC-MS/MS. Data are shown as mean \pm SEM from n=8 mice per group.

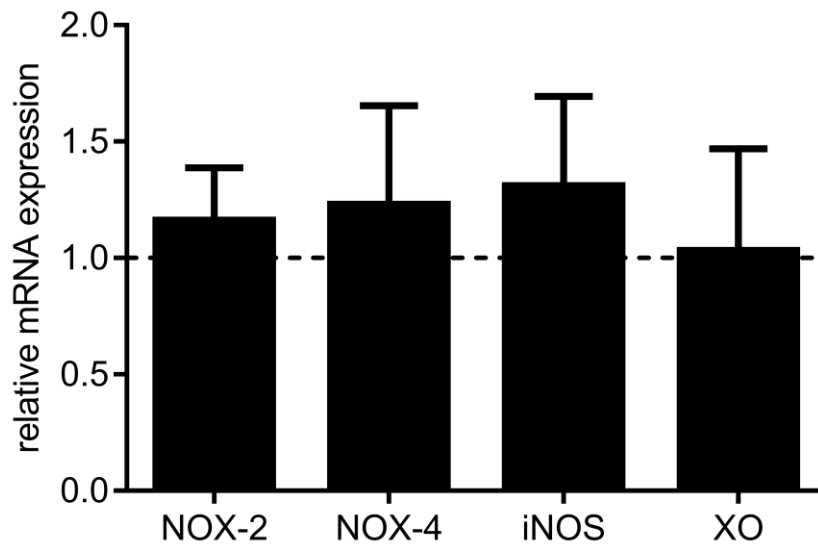


Figure S4: Expression of NADPH-oxidases 2 and 4 (NOX-2 and NOX-4), inducible nitric oxide synthase (iNOS) and xanthine oxidase (XO) in DRGs eight days after paclitaxel treatment. Relative expression levels are normalized to vehicle controls. Data are shown as \pm SEM from n=4-5 mice and analyzed with unpaired student's t-test.

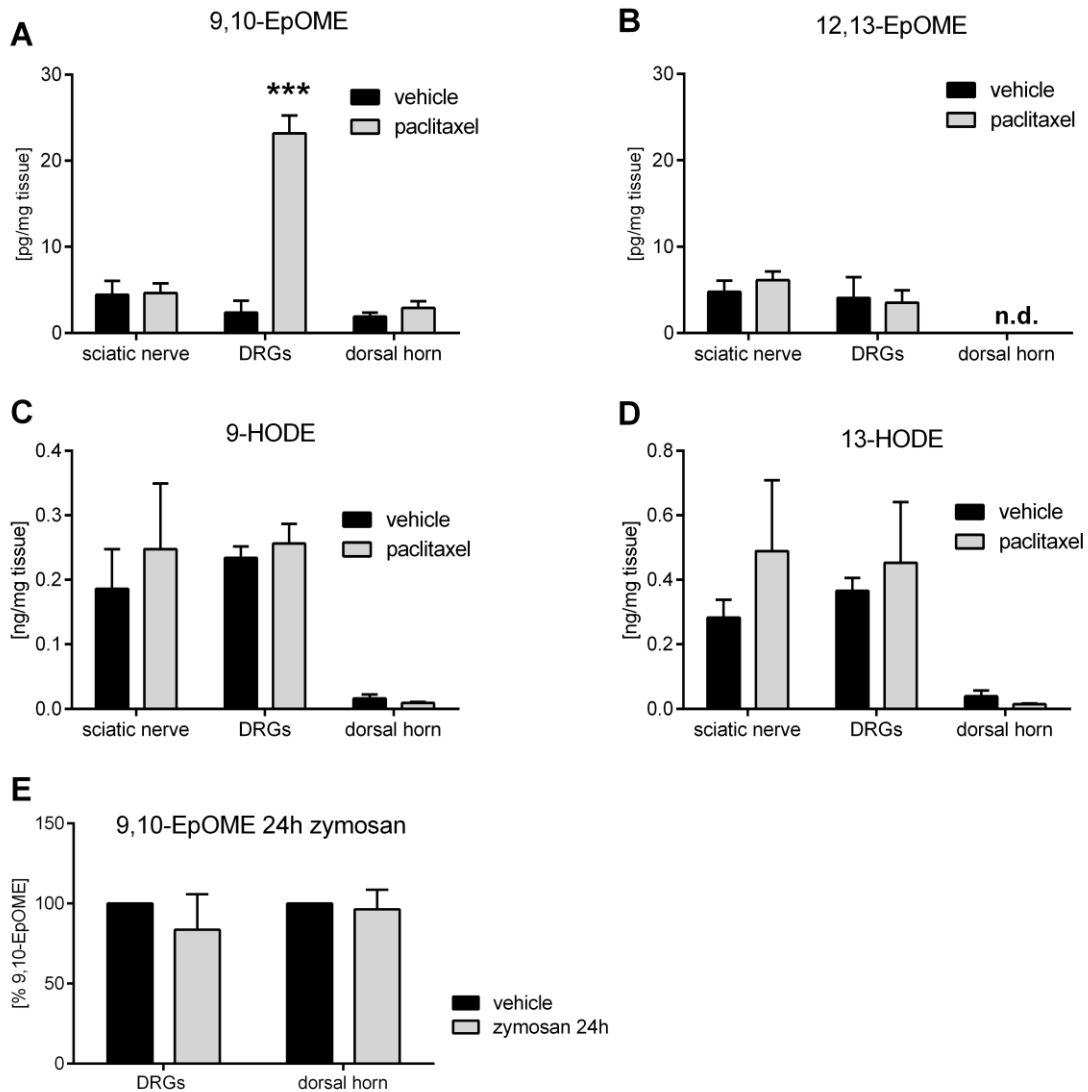


Figure S5: Concentrations of the oxidized linoleic acid metabolites 24h after paclitaxel injection. 9,10-EpOME (A), 12,13-EpOME (B), 9-HODE (C) and 13-HODE (D), in sciatic nerves, lumbar DRGs and the dorsal spinal cord of wild type mice, (6 mg/kg, grey bars). Concentration differences in 9,10-EpOME in lumbar DRGs, 24h after zymosan injection (12.5 mg · ml⁻¹, 10 µl injection volume, grey bars) into the hind paw of wild type mice (E) shown for comparison. Data are means ± SEM from five individual mice per group, n.d.: not determined, ***p<0.001, one-way ANOVA.

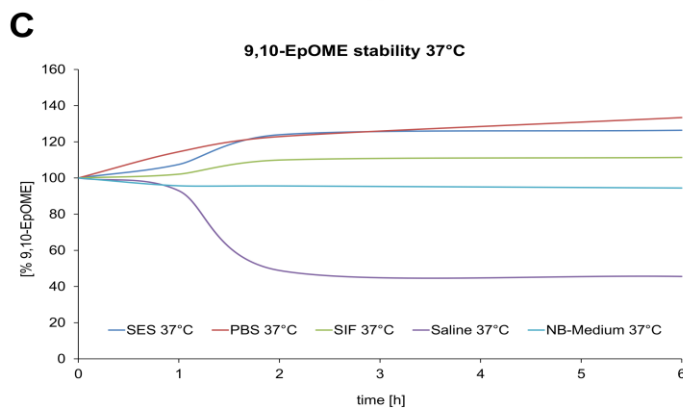
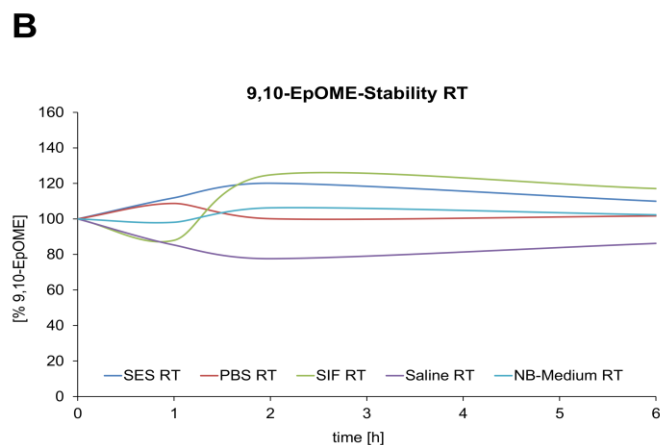
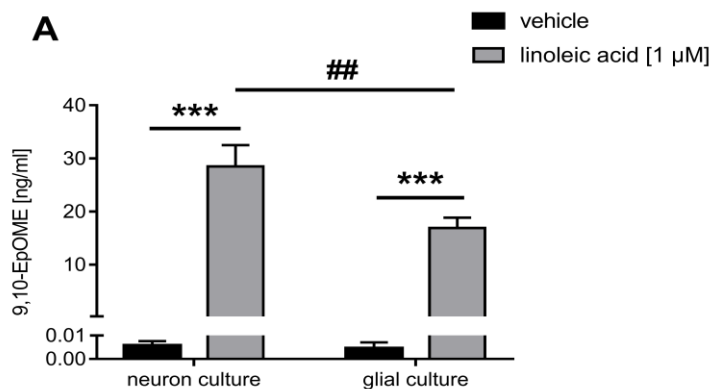


Figure S6: Neuronal vs. Glial-production of 9,10-EpOME and *in vitro* stability of 9,10-EpOME in all buffers used throughout the whole study for up to six hours at room temperature (B) or at 37°C (C). Neuron or glial cultures from n=4 individual mice were stimulated with linoleic acid (1 μ M, 1h, grey) or vehicle (black). EpOME-concentrations were determined by LC-MS/MS; ##p<0.01, ***p<0.001 Two-way ANOVA.

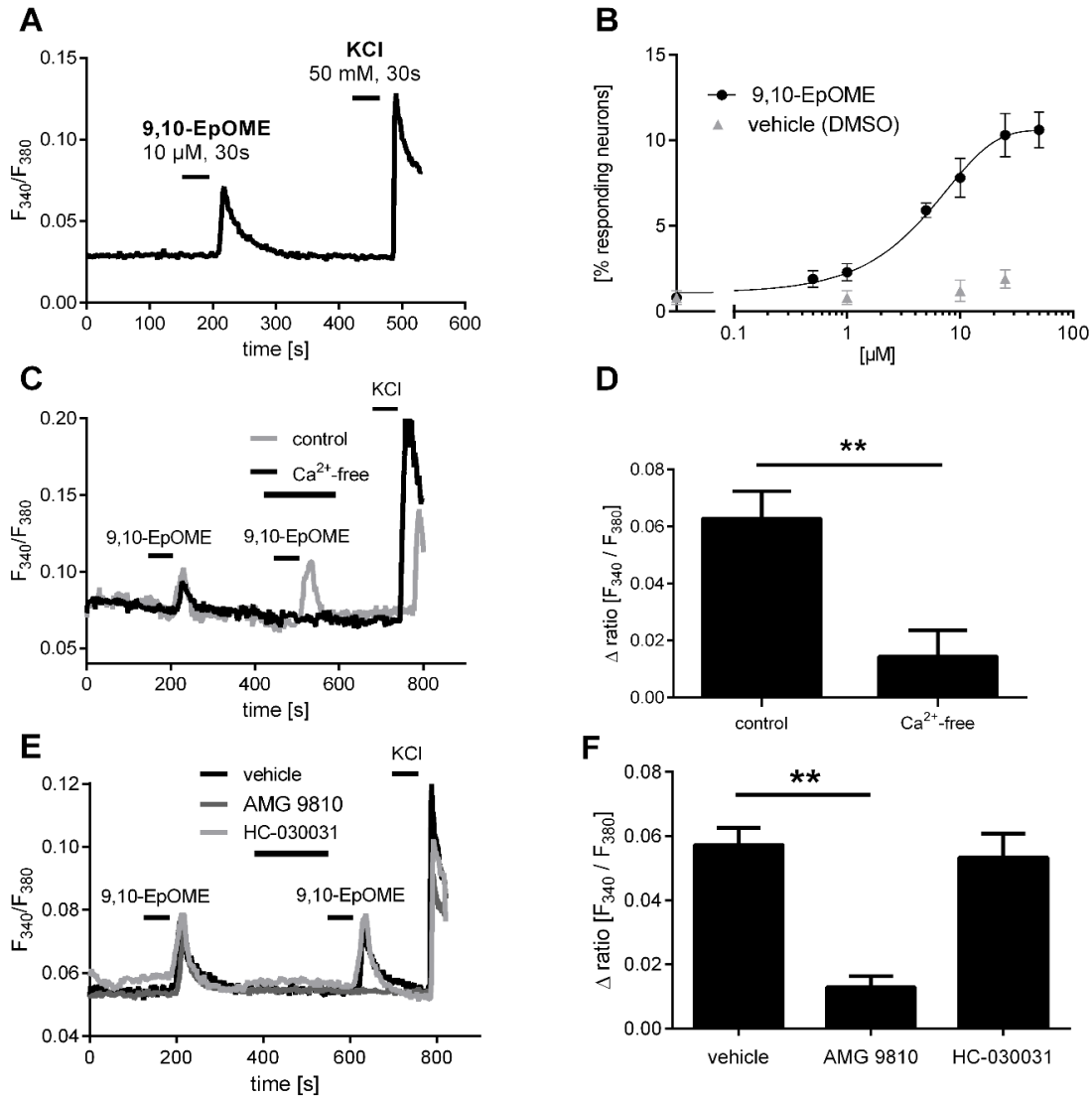


Figure S7: Direct effects of 9,10-EpOME on sensory neurons. 9,10-EpOME [$> 5 \mu\text{M}$] causes calcium transients in up 10.3 % of DRG neurons (**A** and **B**), which can be blocked by calcium-free medium containing 2 mM EGTA (**C** and **D**) or by the presence of the selective TRPV1 antagonist, AMG9810 [$1 \mu\text{M}$], but not the selective TRPA1 antagonist, HC-030031 [$20 \mu\text{M}$] (**E** and **F**). Data represent the means \pm SEM of 16 (control), 31 (AMG 9810) or 18 (HC-030031) neurons; $**p < 0.01$, one-way ANOVA.

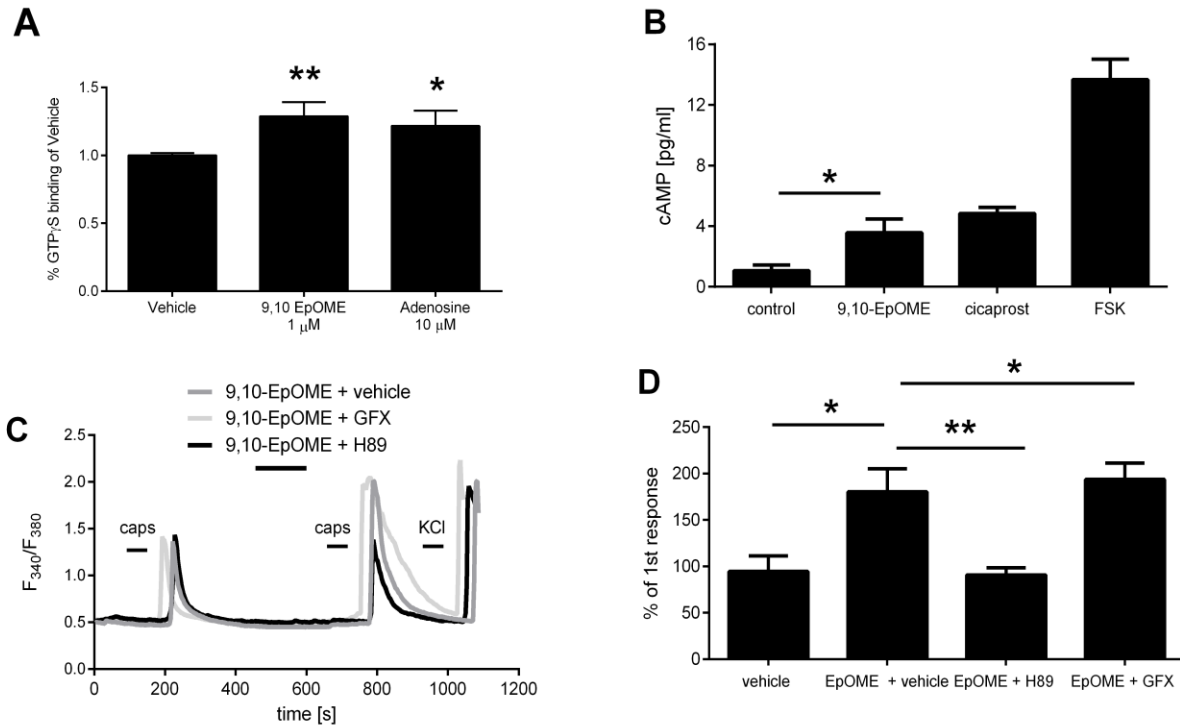


Figure S8: Intracellular signaling of 9,10-EpOME. [γ -³⁵S]-GTP binding assays in membrane fractions of rat DRGs incubated for 30 minutes with GDP (30 μM) adenosine (10 μM), 9,10-EpOME (1 μM) or vehicle (DMSO 0.7% (v/v)). Data represent means of 3 measurements in membrane fractions from a total of 15 animals; * $p < 0.05$, ** $p < 0.01$, Kruskal-Wallis test with Dunn's post hoc test (A). (B) Concentrations of cAMP in neuron-enriched DRG cultures after stimulation for 15 minutes with 9,10-EpOME, cicaprost or forskolin (FSK, 1 μM each). Data represent means \pm SEM of DRG cultures from five mice. (C and D) TRPV1 sensitization by 9,10-EpOME (1 μM, dark grey) after preincubation with a PKA inhibitor (H89 dihydrochloride, 20 μM for 1h, black) or a PKC inhibitor (GF 109203X (GFX), 1 μM for 1h, grey). (D) Statistical analysis of the results from (C). Data represent means \pm SEM of 15-39 neurons, * $p < 0.05$, ** $p < 0.01$, one-way ANOVA; n.s. not significant.

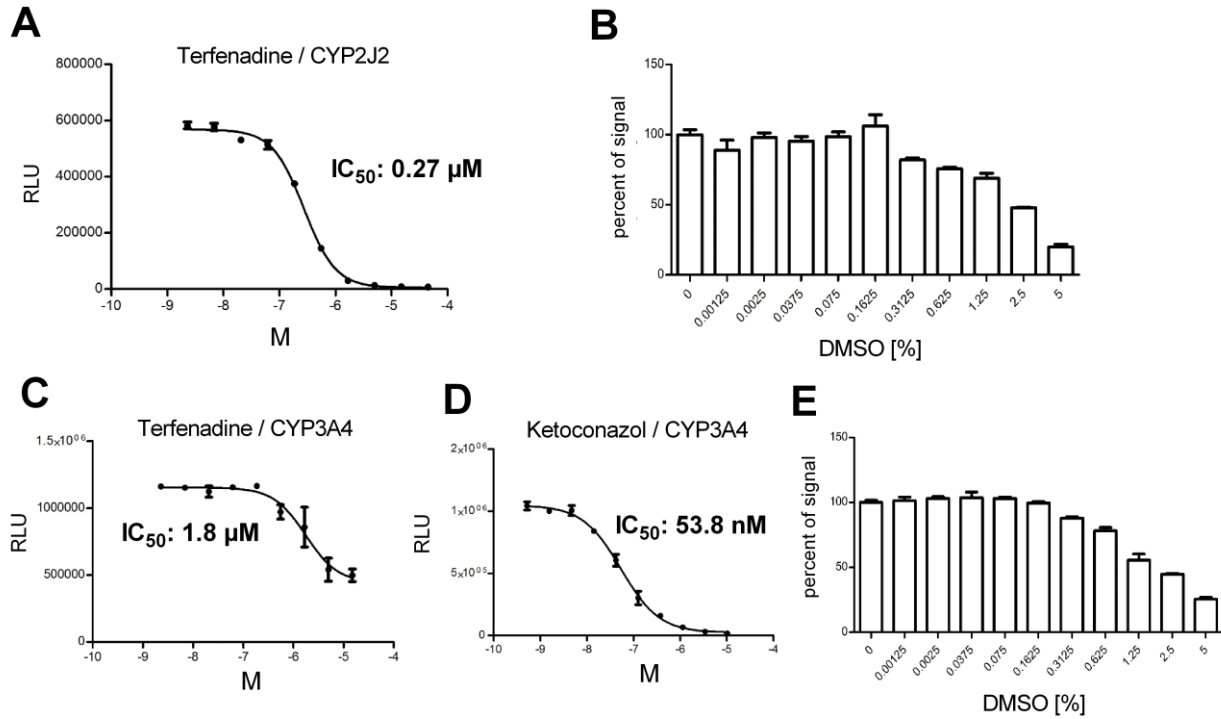


Figure S9: Establishment of CYP2J2 and CYP3A4 inhibition screens with CYP-expressing supersomes using terfenadine (A and C) or ketoconazole (D) as positive controls. Assays were tested for DMSO tolerance and were stable up to 0.5% DMSO (v/v) (B and E).

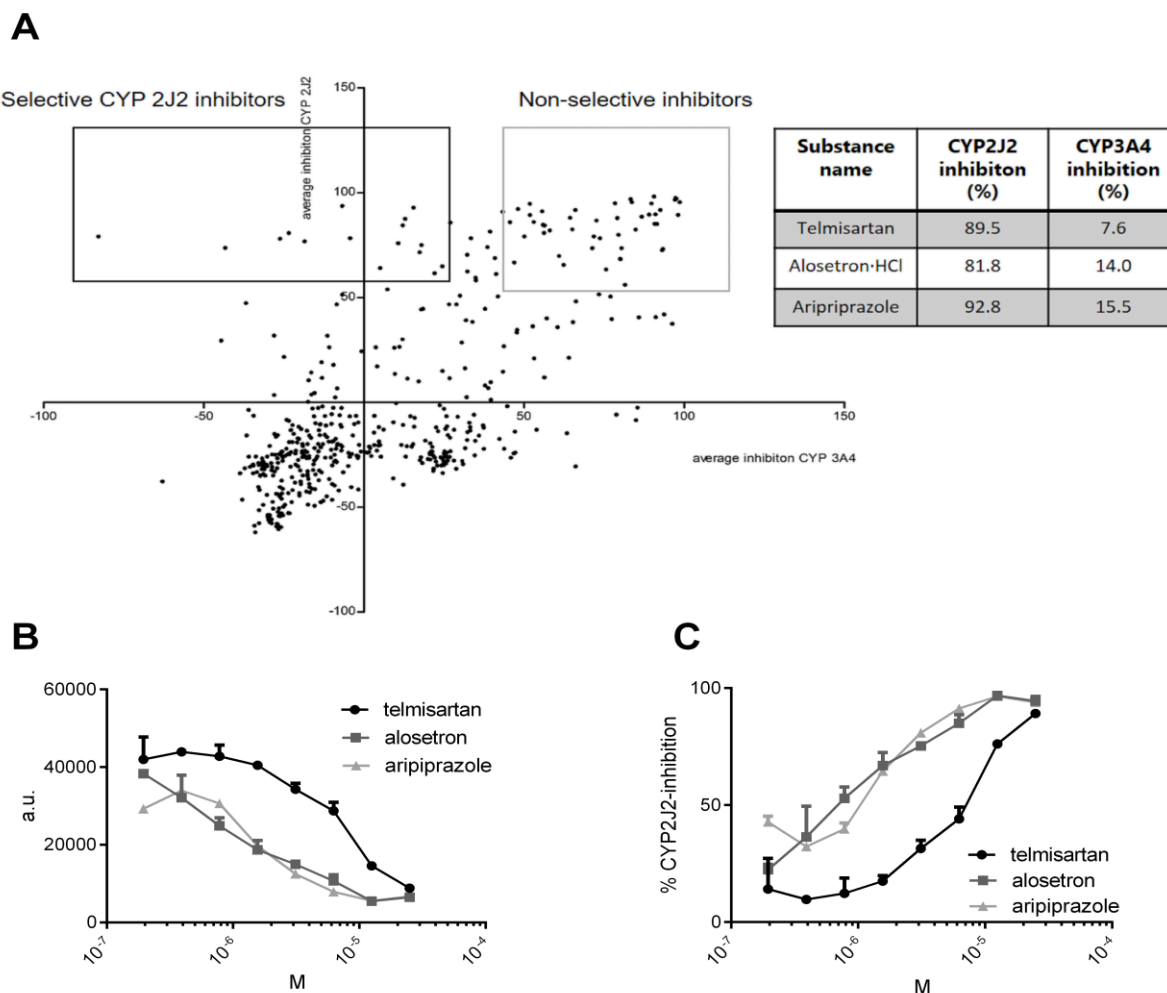


Figure S10: Drug repurposing screen for CYP2J2 inhibitors. (A) Correlation plot of calculated inhibition values of CYP2J2 and CYP3A4. Each dot in (A) represents an approved substance tested in the screen in duplicate at [10 μ M]. Substances with an CYP2J2 inhibition >60% and CYP3A4 inhibition <20% are highlighted in the black box. Unspecific substances are indicated in the grey box. Selected hits with high CYP2J2 inhibition and low CYP3A4 inhibition are shown in the table. Screening hits were validated with CYP2J2 overexpressing HEK-cells (B and C). Here, each concentration or substance was measured in triplicate.

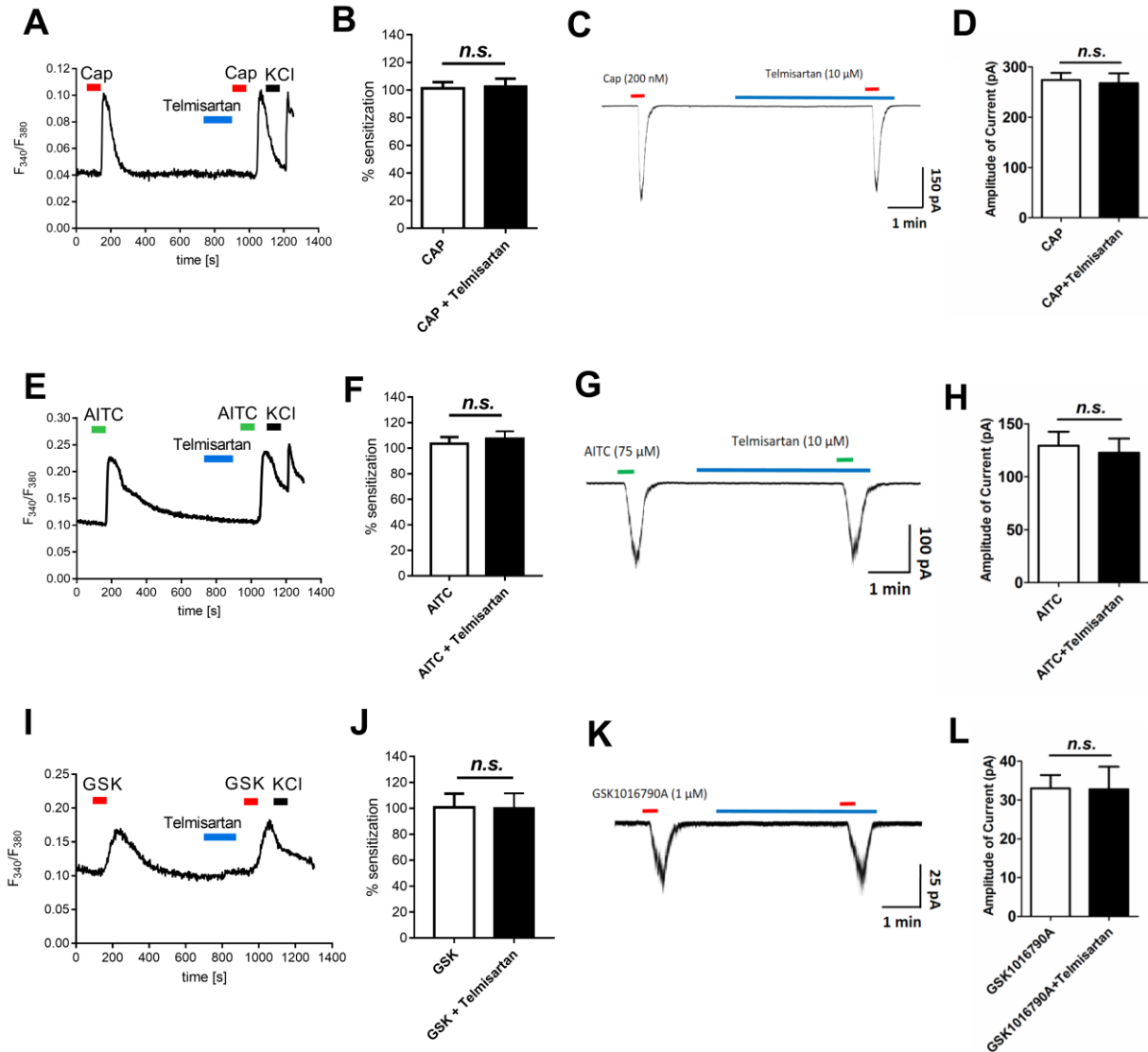


Figure S11: Telmisartan does not affect TRPV1, TRPA1 or TRPV4. Shown are two TRP channel responses of sensory neurons to selective agonists and in-between incubation with telmisartan [10 μ M]. The amplitudes of both responses were compared statistically with the student's t-test. (A, and B) Calcium-Imaging responses to the selective TRPV1 agonist capsaicin (Cap, 200 nM, 15s; n=30-44 neurons) and capsaicin evoked inward currents; n=11 neurons (C and D). (E and F) Calcium-influx after stimulation with the selective TRPA1 agonist AITC (allyl isothiocyanate, 75 μ M, 30s; n=41-

55 neurons) and inward currents of AITC stimulated neurons (n=10 neurons; G and H). (I and J) Responses of DRG cells to the selective TRPV4-agonist GSK1016790A (GSK, 1 μ M, 30s, n=50-51 cells) and inward currents of n=4 neurons stimulated with GSK (K and L). Notably, most TRPV4 responding cells were glial cells and only 10% of sensory neurons responded to the TRPV4 agonist GSK (4/40 neurons).

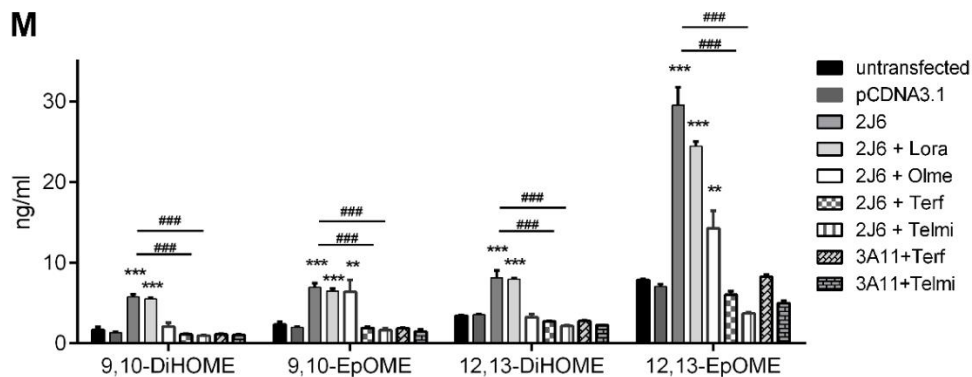
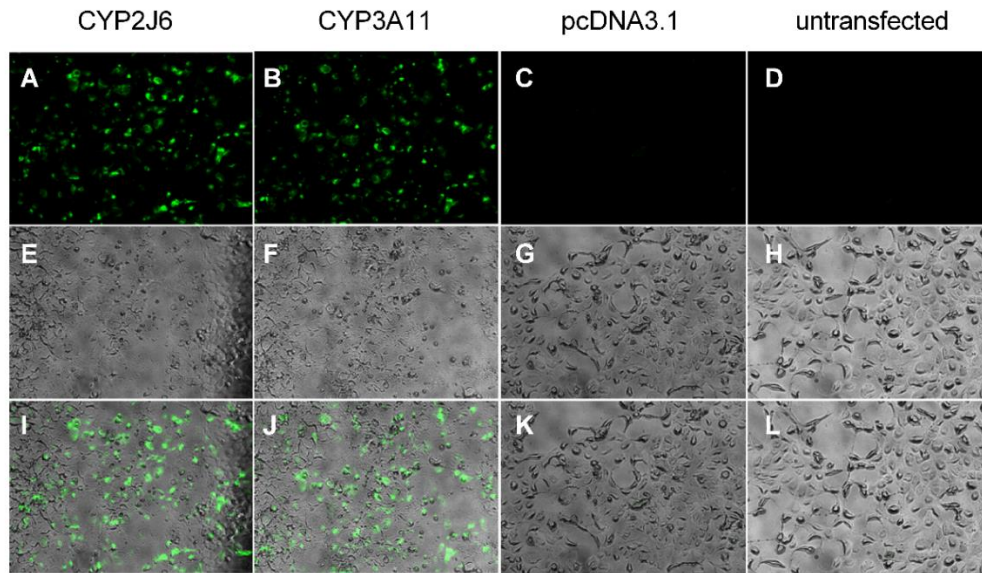


Figure S12: Expression controls of CYPs in HEK-293 cells and lipid concentrations after stimulation with linoleic acid. GFP expression in HEK-293 cells after transfection with CYP2J6 or CYP3A11 for 48h (A-I). (M) Concentrations of 9,10-EpOME,9,10-DiHOME, 12,13-EpOME and 12,13-DiHOME in supernatants of HEK-293 cells untransfected or transfected with pcDNA3.1, CYP2J6 or CYP3A11 for 48h and stimulated with linoleic acid (1 μ M, 1h) and either, 5 μ M terfenadine (terf), 5 μ M loratadine (lora), 10 μ M telmisartan (telmi) or 10 μ M olmesartan (olme). For each condition, three wells of a 6-well plate were used, data are shown as means \pm SEM; **p<0.01, ***,###p<0.001, one way ANOVA.

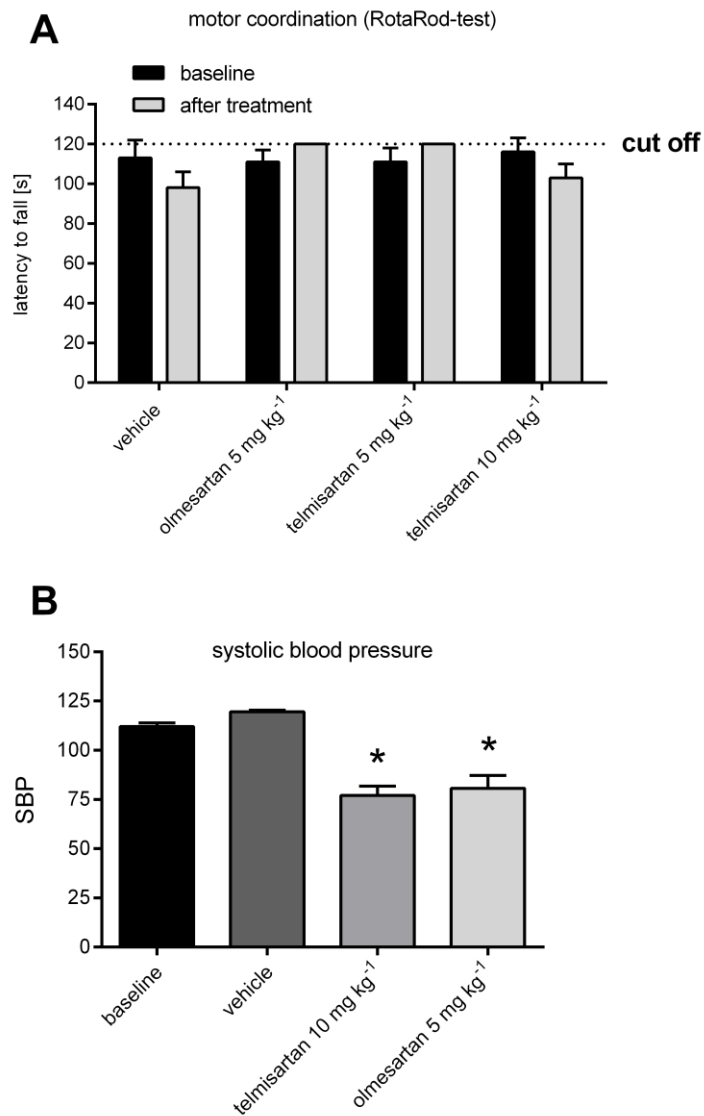


Figure S13: Motor coordination and blood pressure in mice after treatment with telmaisartan. (A) Motor coordination of wild type BL/6N mice tested in the RotaRod test at 16 rpm. The cut-off time was set at 120 seconds. (B) systolic blood pressure of wild type BL/6N mice. Mice were injected either vehicle, olmesartan (5 mg/kg i.p.), or telmisartan (5 or 10 mg/kg i.p. (A) or 10 mg/kg (B)) 2h before the measurement. Data are presented as means \pm SEM from 4-10 mice per group, * $p < 0.05$ one-way ANOVA compared to baseline.

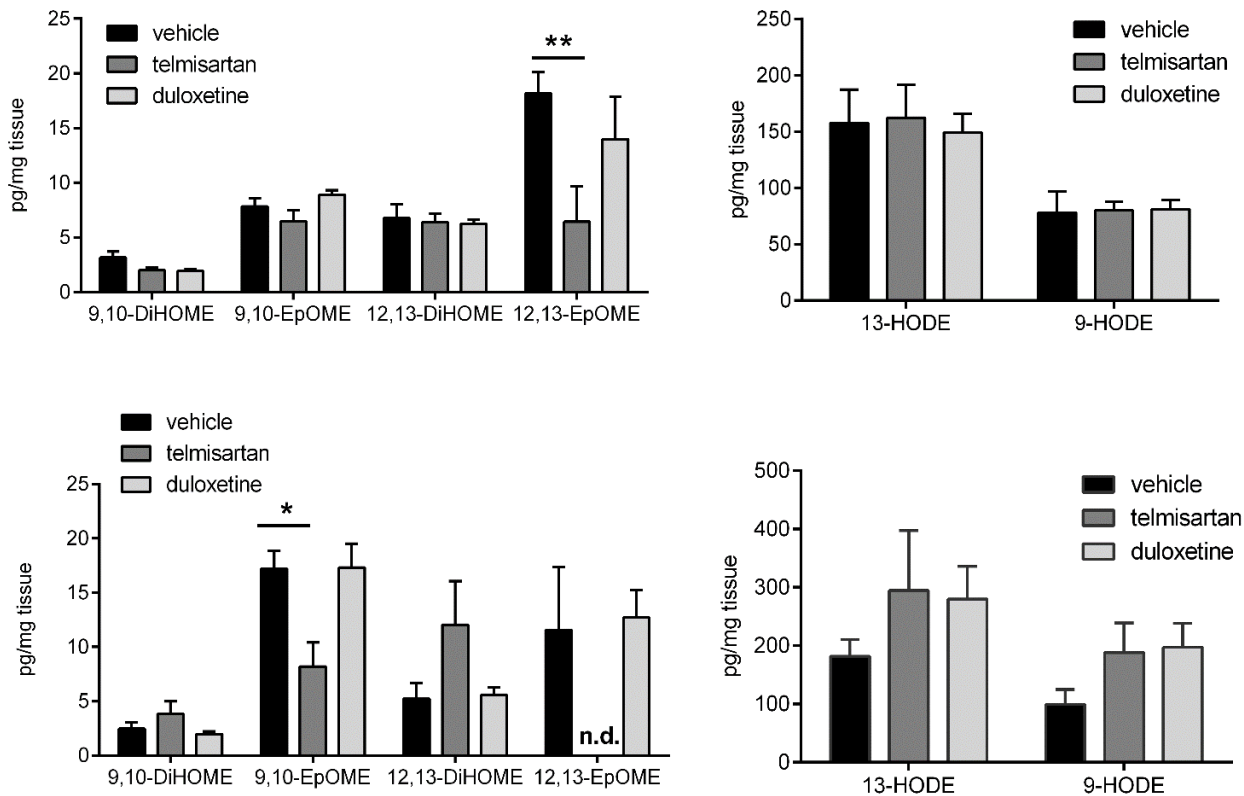


Figure S14: OLAMs synthesis during PIPN after treatment with duloxetine or telmisartan. Concentrations, of the oxidized linoleic acid metabolites, 9,10-EpOME, 12,13-EpOME, 9-HODE and 13-HODE in sciatic nerves (upper) and lumbar DRGs (lower) of wild type mice 8d after paclitaxel-injection (6 mg/kg), treated with telmisartan (5 mg/kg) or duloxetine (10 mg/kg) every second day. Data are shown as means \pm SEM from six individual mice per group, n.d.: not determined, * $p < 0.05$, ** $p < 0.01$, one-way ANOVA.

Table S1a: Lipid concentrations, 8d after paclitaxel injection, in sciatic nerves from wild type mice (n=6 per group), CYP: cytochrome P450-epoxygenase, LOX: lipoxygenase, COX: cyclooxygenase, PG: prostaglandin, LT: leukotriene.

sciatic nerve	High dose paclitaxel (HD, 6 mg/kg)					Multiple low dose paclitaxel (MLD, 4 x 2 mg/kg)				
	vehicle		paclitaxel		p-value	vehicle		paclitaxel		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM	pg lipid/mg	SEM	
CYP										
9,10-EpOME	1.92	0.61	2.8	0.60	> 0.05	0.81	0.33	1.51	0.58	> 0.05
9,10-DiHOME	3.94	0.97	4.6	1.22	> 0.05	4.22	0.61	4.4	0.54	> 0.05
12,13-EpOME	11.8	2.52	9.0	0.92	> 0.05	17.3	3.40	19.2	2.99	> 0.05
12,13-DiHOME	16.1	1.91	18.0	2.27	> 0.05	13.3	2.02	15.5	1.53	> 0.05
9-HODE	373.3	56.1	118.9	26.5	> 0.05	374.7	60.4	315.9	19.4	> 0.05
13-HODE	328.5	65.4	334.7	35.0	> 0.05	351.1	56.9	280.8	29.9	> 0.05
14,15-EET	36.7	9.3	39.1	10.2	> 0.05	n.d	n.d	n.d	n.d	n.d.
LOX										
5-HETE	32.5	2.7	37.2	5.1	> 0.05	40.4	12.9	46.9	6.0	> 0.05
12-HETE	9.6	3.6	8.3	1.7	> 0.05	5.3	0.9	4.4	0.9	> 0.05
15-HETE	225.0	41.9	164.8	22.9	> 0.05	130.4	32.1	97.4	9.9	> 0.05
20-HETE	13.6	3.0	8.2	0.7	> 0.05	10.7	0.3	10.7	1.1	> 0.05
LTB ₄	2.3	0.5	1.6	0.3	> 0.05	n.d	n.d	n.d	n.d	n.d.
COX										
PGE ₂	93.4	13.5	71.6	13.3	> 0.05	66.8	16.8	69.2	11.2	> 0.05
PGD ₂	148.1	28.5	74.1	20.2	> 0.05	141.0	5.7	141.8	2.4	> 0.05
6-keto-PGF _{1α}	56.9	12.4	57.1	16.5	> 0.05	39.3	8.2	44.0	4.9	> 0.05
PGF _{2α}	30.1	6.4	21.0	3.6	> 0.05	18.6	3.1	21.4	2.5	> 0.05
TXB ₂	23.2	6.3	24.7	4.4	> 0.05	35.8	5.3	29.8	7.5	> 0.05

Table S1b: Lipid concentrations, 8d after paclitaxel injection, in lumbar DRGs from wild-type mice (n=6 per group). Significant differences from vehicle are highlighted, n.d: not determined, *p<0.05, **p<0.01, one-way ANOVA.

lumbar DRGs	High dose paclitaxel (HD, 6 mg/kg)					Multiple low dose paclitaxel (MLD, 4 x 2 mg/kg)				
	vehicle		paclitaxel		p-value	vehicle		paclitaxel		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM	pg lipid/mg	SEM	
CYP										
9,10-EpOME	19.3	5.1	41.5	5.4	** < 0.01	38.5	5.8	65.2	7.3	* < 0.05
9,10-DiHOME	16.5	3.3	13.1	2.3	> 0.05	12.8	1.7	11.3	0.8	> 0.05
12,13-EpOME	26.2	5.5	34.8	8.0	> 0.05	14.3	5.8	26.1	8.4	> 0.05
12,13-DiHOME	26.3	2.4	24.5	2.3	> 0.05	11.7	2.2	10.5	1.9	> 0.05
9-HODE	227.4	27.5	245.0	10.4	> 0.05	218.8	31.7	181.3	15.2	> 0.05
13-HODE	385.6	47.6	446.5	32.8	> 0.05	245.1	28.3	203.1	22.9	> 0.05
14,15-EET	2630.6	511.1	3110.1	425.8	> 0.05	n.d	n.d	n.d	n.d	n.d.
LOX										
5-HETE	51.3	10.1	35.5	6.0	> 0.05	17.7	5.2	25.9	1.8	> 0.05
12-HETE	24.5	5.3	8.1	1.9	** < 0.01	26.3	8.9	41.3	13.5	> 0.05
15-HETE	143.3	14.5	102.0	8.8	* < 0.05	91.1	19.1	96.5	2.9	> 0.05
20-HETE	38.9	5.2	32.7	2.8	> 0.05	34.3	8.3	31.6	4.5	> 0.05
LTB₄	5.4	1.2	3.7	0.9	> 0.05	n.d	n.d	n.d	n.d	n.d.
COX										
PGE₂	321.6	47.0	271.2	26.2	> 0.05	311.2	43.1	242.1	56.0	> 0.05
PGD₂	639.4	169.9	468.8	39.9	> 0.05	342.7	37.7	273.3	50.5	> 0.05
6-keto-PGF_{1α}	584.0	33.1	465.1	29.1	* < 0.05	608.2	34.7	319.5	45.7	** < 0.01
PGF_{2α}	114.0	17.2	85.6	16.3	> 0.05	117.2	20.5	84.7	28.0	> 0.05
TXB₂	59.5	5.8	71.0	8.9	> 0.05	78.5	13.9	53.1	14.1	> 0.05

Table S1c: Lipid concentrations, 8d after paclitaxel injection, in the spinal dorsal horn from wild-type mice (n=6 per group). Significant differences from vehicle are highlighted, n.d: not determined, *p<0.05, one-way ANOVA.

dorsal horn day 8	High dose paclitaxel (HD, 6 mg/kg)					Multiple low dose paclitaxel (MLD, 4 x 2 mg/kg)				
	vehicle		paclitaxel		p-value	vehicle		paclitaxel		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM	pg lipid/mg	SEM	
CYP										
9,10-EpOME	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
9,10-DiHOME	6.6	0.8	5.8	1.1	> 0.05	0.7	0.3	0.3	0.2	> 0.05
12,13-EpOME	8.0	1.2	5.5	0.9	> 0.05	6.3	1.4	5.6	1.3	> 0.05
12,13-DiHOME	1.3	0.6	1.6	0.7	> 0.05	2.6	0.7	2.5	0.2	> 0.05
9-HODE	58.0	11.8	42.7	7.1	> 0.05	41.3	5.6	40.5	4.9	> 0.05
13-HODE	80.3	16.7	66.3	12.4	> 0.05	64.3	7.4	57.0	4.2	> 0.05
14,15-EET	231.8	55.2	271.3	65.0	> 0.05	n.d.	n.d.	n.d.	n.d.	n.d.
LOX										
5-HETE	18.7	5.3	17.3	2.6	> 0.05	4.3	0.5	4.3	0.8	> 0.05
12-HETE	10.5	3.6	2.9	0.8	* < 0.05	14.8	2.3	10.9	3.2	> 0.05
15-HETE	35.6	3.7	27.3	4.4	> 0.05	29.6	3.3	30.3	6.3	> 0.05
20-HETE	3.9	0.8	5.0	0.8	> 0.05	1.3	0.1	1.6	0.5	> 0.05
LTB₄	7.2	2.4	4.7	0.8	> 0.05	n.d.	n.d.	n.d.	n.d.	n.d.
COX										
PGE₂	78.2	23.2	70.8	6.7	> 0.05	121.4	27.6	173.3	25.9	> 0.05
PGD₂	243.8	65.2	355.9	55.2	> 0.05	174.0	41.7	251.1	44.9	> 0.05
6-keto-PGF_{1α}	62.7	29.7	124.9	38.9	> 0.05	66.3	44.1	116.2	55.8	> 0.05
PGF_{2α}	130.3	49.4	195.5	16.6	> 0.05	117.2	19.1	144.9	48.3	> 0.05
TXB₂	93.4	17.9	102.2	11.6	> 0.05	73.3	15.9	100.2	13.6	> 0.05

Table S1d: Endocannabinoid/endovanilloid concentrations, 8d after paclitaxel injection, in lumbar DRGs (left) and the spinal dorsal horn (right) from wild-type mice (n=8 per group). AEA: anandamide, PEA: palmitoylethanolamide, OEA: oleoylethanolamide, NADA: N-arachidonoyl dopamine, 1-AG and 2-AG: 1- and 2-arachidonoylglycerol, 1-OG: 1-oleoylglycerol. Data were analyzed with One-way ANOVA.

	lumbar DRGs					spinal dorsal horn				
	vehicle		paclitaxel 6mg/kg		p-value	vehicle		paclitaxel 6mg/kg		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM	pg lipid/mg	SEM	
Ethanol-amides										
AEA	44.1	3.63	52.4	0.60	> 0.05	51.6	2.72	49.1	2.02	> 0.05
PEA	119.8	14.3	170.8	1.22	> 0.05	418.6	28.3	457.1	26.4	> 0.05
OEA	77.7	4.17	94.3	0.92	> 0.05	163.8	11.2	188.7	13.7	> 0.05
Endo-vanilloid										
NADA	7.1	0.75	9.0	5.1	> 0.05	6.9	0.64	8.2	1.06	> 0.05
Monoacylglycerols										
1-AG	276.6	63.5	389.7	65.2	> 0.05	213.6	46.4	324.4	49.0	> 0.05
2-AG	2781.4	257.5	3285.4	530.0	> 0.05	4096.4	426.7	4785.2	523.8	> 0.05
1-OG	2567.4	415.8	3020.5	424.6	> 0.05	1757.9	315.3	2687.4	424.6	> 0.05

Table S2a: Lipid concentrations, 8d after paclitaxel injection, in sciatic nerves from wild type mice following administration of terfenadine, loratadine, telmisartan or olmesartan for two hours (n=6 per group). CYP: cytochrome P450-epoxygenase, LOX: lipoxygenase, COX: cyclooxygenase, PG: prostaglandin, LT: leukotriene. Significant differences from vehicle are highlighted, *p<0.05, one-way ANOVA.

sciatic nerve	High dose paclitaxel (HD, 6 mg/kg) 8d													
	vehicle 2h i.p.		terfenadine 1 mg · kg ⁻¹ i.p., 2h		p-value	loratadine 1 mg · kg ⁻¹ i.p., 2h		p-value	telmisartan 5 mg · kg ⁻¹ i.p., 2h		p-value	olmesartan 5 mg · kg ⁻¹ i.p., 2h		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM	
CYP														
9,10-EpOME	2.29	0.43	2.8	1.15	> 0.05	2.61	0.69	> 0.05	4.46	1.5	> 0.05	3.44	0.74	> 0.05
9,10-DiHOME	3.69	1.56	2.97	0.83	> 0.05	2.98	0.66	> 0.05	5.48	1.72	> 0.05	3.01	0.39	> 0.05
12,13-EpOME	8.39	2.71	12.7	2.09	> 0.05	5.52	1.71	> 0.05	8.68	1.34	> 0.05	8.32	2.03	> 0.05
12,13-DiHOME	28	6.35	20.1	4.17	> 0.05	18.6	2.63	> 0.05	22.2	2.96	> 0.05	12.7	3.85	* < 0.05
9-HODE	338.2	56.6	288.3	46.5	> 0.05	390.8	26.7	> 0.05	266	62.6	> 0.05	297.3	31.4	> 0.05
13-HODE	383.7	73.1	345.8	33.2	> 0.05	387.1	24.3	> 0.05	294.3	58.7	> 0.05	389.7	31.9	> 0.05
14,15-EET	33.4	8.39	22.8	5.4	> 0.05	24.7	1.84	> 0.05	24.1	4.22	> 0.05	41.9	11.3	> 0.05
LOX														
5-HETE	27.8	5.83	37.9	6.19	> 0.05	32.7	5.41	> 0.05	33.2	3.06	> 0.05	33.4	4.36	> 0.05
12-HETE	8.73	2.44	5.09	1.31	> 0.05	12.1	1.11	> 0.05	7.41	1.36	> 0.05	6.30	1.41	> 0.05
15-HETE	158.4	39.9	203.6	48.3	> 0.05	188.3	21.4	> 0.05	189.7	38.3	> 0.05	181.4	21.4	> 0.05
20-HETE	16.8	1.47	19.8	2.63	> 0.05	20.2	2.56	> 0.05	11.0	2.71	> 0.05	16.5	1.11	> 0.05
LTB ₄	1.67	0.63	2.05	0.61	> 0.05	2.73	0.82	> 0.05	0.99	0.34	> 0.05	1.91	0.27	> 0.05
COX														
PGE ₂	59.5	5.60	80.9	21.8	> 0.05	71.2	8.31	> 0.05	81.0	19.4	> 0.05	73.2	13.7	> 0.05
PGD ₂	42.1	9.39	60.8	7.97	> 0.05	52.8	6.33	> 0.05	72.3	5.3	> 0.05	28.6	9.24	> 0.05
6-keto-PGF _{1α}	45.5	2.59	74.5	31.5	> 0.05	38.4	7.20	> 0.05	61.8	4.8	> 0.05	48.7	1.52	> 0.05
PGF _{2α}	18.8	3.41	27.8	11.03	> 0.05	25.5	5.04	> 0.05	20.7	2.1	> 0.05	16.8	5.23	> 0.05
TXB ₂	35.6	12.2	34.4	14.1	> 0.05	28.9	4.11	> 0.05	33.2	1.6	> 0.05	15.9	3.15	* < 0.05

Table S2b: Lipid concentrations, 8d after paclitaxel injection, in lumbar DRGs from wild type mice following administration of terfenadine, loratadine, telmisartan or olmesartan for two hours (n=6 per group). Significant differences from vehicle are highlighted, *p<0.05, one-way ANOVA.

lumbar DRGs	High dose paclitaxel (HD, 6 mg/kg) 8d													
	vehicle 2h i.p.		terfenadine 1 mg · kg ⁻¹ i.p., 2h		p-value	loratadine 1 mg · kg ⁻¹ i.p., 2h		p-value	telmisartan 5 mg · kg ⁻¹ i.p., 2h		p-value	olmesartan 5 mg · kg ⁻¹ i.p., 2h		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM	
CYP														
9,10-EpOME	11.2	1.5	4.89	0.83	* < 0.05	10.4	1.99	> 0.05	5.61	0.96	* < 0.05	9.8	2.16	> 0.05
9,10-DiHOME	6.9	0.65	5.38	1.44	> 0.05	5.55	0.67	> 0.05	n.d	n.d	n.d	5.55	0.69	> 0.05
12,13-EpOME	13.35	1.41	9.03	0.31	* < 0.05	15.4	2.25	> 0.05	12.86	1.55	> 0.05	13.03	0.42	> 0.05
12,13-DiHOME	24.9	3.4	19.4	2.91	> 0.05	17.8	6.64	> 0.05	20.1	1.11	> 0.05	15.7	6.88	> 0.05
9-HODE	630.5	95.2	567.5	78.0	> 0.05	611.0	109.5	> 0.05	193.4	12.8	* < 0.05	502.4	81.5	> 0.05
13-HODE	784.3	171.1	585.8	78.1	> 0.05	967.2	185.6	> 0.05	279.9	22.7	* < 0.05	967.2	227.6	> 0.05
14,15-EET	211.5	44.8	232.8	47.7	> 0.05	202	21.9	> 0.05	188.1	23.2	> 0.05	223.9	33.1	> 0.05
LOX														
5-HETE	41.8	4.84	31.7	7.44	> 0.05	33.0	6.53	> 0.05	46.3	41.9	> 0.05	39.8	3.96	> 0.05
12-HETE	7.79	1.92	6.19	1.03	> 0.05	9.44	1.21	> 0.05	12.1	2.32	> 0.05	11.4	2.06	> 0.05
15-HETE	119.8	13.1	114.5	11.5	> 0.05	104.2	20.9	> 0.05	123.9	9.72	> 0.05	108.6	12.0	> 0.05
20-HETE	33.3	8.10	48.6	9.86	> 0.05	38.8	4.24	> 0.05	36.3	2.73	> 0.05	27.9	4.23	> 0.05
LTB ₄	3.90	0.79	3.35	0.47	> 0.05	4.12	1.16	> 0.05	5.05	1.13	> 0.05	3.38	0.58	> 0.05
COX														
PGE ₂	208.6	101.9	374.7	77.2	> 0.05	289.6	44.3	> 0.05	242.9	23.9	> 0.05	330.1	8.79	> 0.05
PGD ₂	270.5	65.4	360.3	81.9	> 0.05	277.1	50.2	> 0.05	328.2	23.8	> 0.05	389.4	70.9	> 0.05
6-keto-PGF _{1α}	555.6	219.9	814.3	114.3	> 0.05	661.5	97.4	> 0.05	594.9	11.3	> 0.05	615.5	25.5	> 0.05
PGF _{2α}	51.9	17.2	85.8	27.9	> 0.05	77.3	26.3	> 0.05	67.4	4.44	> 0.05	86.5	31.4	> 0.05
TXB ₂	87.6	23.3	147.7	34.2	> 0.05	76.1	21.0	> 0.05	81.8	30.6	> 0.05	112.7	15.2	> 0.05

Table S2c: Lipid concentrations, 8d after paclitaxel injection, in the spinal dorsal horn from wild type mice following administration of terfenadine, loraratadine, telmisartan or olmesartan for two hours (n=6 per group). Significant differences to vehicle are highlighted, *p<0.05, one-way ANOVA.

dorsal horn	High dose paclitaxel (HD, 6 mg/kg) 8d													
	vehicle 2h i.p.		terfenadine 1 mg · kg ⁻¹ i.p., 2h		p-value	loratidine 1 mg · kg ⁻¹ i.p., 2h		p-value	telmisartan 5 mg · kg ⁻¹ i.p., 2h		p-value	olmesartan 5 mg · kg ⁻¹ i.p., 2h		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM	
CYP														
9,10-EpOME	1.08	0.13	1.55	0.37	> 0.05	0.95	0.33	> 0.05	1.2	0.15	> 0.05	0.91	0.23	> 0.05
9,10-DiHOME	11.5	2.84	12.62	0.63	> 0.05	11.95	0.21	> 0.05	8.21	2.42	> 0.05	6.74	2.15	> 0.05
12,13-EpOME	5.48	0.92	4.05	0.25	> 0.05	6.39	0.91	> 0.05	8.55	2.03	> 0.05	6.22	1.33	> 0.05
12,13-DiHOME	2.71	0.64	2.72	0.38	> 0.05	2.83	0.77	> 0.05	2.45	0.46	> 0.05	1.78	0.56	> 0.05
9-HODE	28.8	3.85	36.5	7.18	> 0.05	36.5	3.94	> 0.05	31.6	5.59	> 0.05	30.3	5.14	> 0.05
13-HODE	37.7	10	43.0	5.63	> 0.05	41.4	4.89	> 0.05	39.7	6.93	> 0.05	28.9	7.20	> 0.05
14,15-EET	214.7	34.8	203	75.2	> 0.05	211.9	31.6	> 0.05	291.2	81.1	> 0.05	302.2	88.3	> 0.05
LOX														
5-HETE	15.5	2.68	14.0	2.97	> 0.05	11.2	1.98	> 0.05	12.3	2.81	> 0.05	12.9	1.81	> 0.05
12-HETE	2.66	0.93	7.59	1.41	* < 0.05	4.11	0.92	> 0.05	5.40	1.70	> 0.05	5.87	1.93	> 0.05
15-HETE	27.8	7.83	37.9	6.19	> 0.05	34.8	5.23	> 0.05	33.2	3.36	> 0.05	33.4	4.64	> 0.05
20-HETE	4.72	0.65	4.52	0.58	> 0.05	4.93	1.16	> 0.05	3.95	0.42	> 0.05	3.90	1.23	> 0.05
LTB ₄	4.01	0.71	5.74	1.25	> 0.05	3.74	0.81	> 0.05	5.40	1.37	> 0.05	5.13	1.42	> 0.05
COX														
PGE ₂	44.5	14.8	46.8	11.2	> 0.05	61.3	9.81	> 0.05	40.6	19.8	> 0.05	69.8	13.1	> 0.05
PGD ₂	233.2	9.60	251.5	65.8	> 0.05	208.8	31.3	> 0.05	189.9	55.2	> 0.05	265.7	35.9	> 0.05
6-keto-PGF _{1α}	70.3	28.1	95.3	27.1	> 0.05	112.7	25.1	> 0.05	94.0	28.2	> 0.05	128.4	31.6	> 0.05
PGF _{2α}	112.6	29.4	129.6	11.7	> 0.05	129.2	26.6	> 0.05	117.7	31.5	> 0.05	144.4	5.42	> 0.05
TXB ₂	81.8	20.6	108.6	9.08	> 0.05	113.9	28.4	> 0.05	88.5	32.6	> 0.05	115.5	11.6	> 0.05

Table S2d: Lipid concentrations, 8d after paclitaxel injection, in the plasma of wild type mice following administration of terfenadine, loratadine, telmisartan or olmesartan for two hours (n=6 animals per group). n.d.: not determined. Significant differences from vehicle are highlighted, *p<0.05, one-way ANOVA.

plasma	High dose paclitaxel (HD, 6 mg/kg) 8d													
	vehicle 2h i.p.		terfenadine 1 mg · kg ⁻¹ i.p., 2h		p-value	loratidine 1 mg · kg ⁻¹ i.p., 2h		p-value	telmisartan 5 mg · kg ⁻¹ i.p., 2h		p-value	olmesartan 5 mg · kg ⁻¹ i.p., 2h		p-value
	pg lipid/mg	SEM	pg lipid/mg	SEM		pg lipid/ mg	SEM		pg lipid/mg	SEM		pg lipid/mg	SEM	
CYP														
9,10- EpOME	0.89	0.14	0.52	0.16	* < 0.05	0.79	0.09	> 0.05	0.5	0.14	* < 0.05	0.70	0.11	> 0.05
9,10- DiHOME	6.9	0.65	3.20	0.47	* < 0.05	4.40	1.16	> 0.05	3.57	0.68	* < 0.05	6.11	0.81	> 0.05
12,13- EpOME	20.4	3.13	10.78	2.12	* < 0.05	24.24	3.58	> 0.05	16.7	1.16	> 0.05	25.5	4.47	> 0.05
12,13- DiHOME	20.2	1.15	12.7	1.4	> 0.05	19.2	3.84	> 0.05	17.5	2.44	> 0.05	17.2	3.24	> 0.05
9-HODE	15.2	1.65	9.66	0.87	* < 0.05	17.4	2.14	> 0.05	8.4	0.65	* < 0.05	17.4	1.73	> 0.05
13-HODE	41.2	0.25	43.6	4.15	> 0.05	44.8	6.37	> 0.05	44.7	2.5	> 0.05	51.1	9.12	> 0.05
14,15- EET	7.34	1.1	7.9	2.3	> 0.05	6.41	0.46	> 0.05	4.2	0.8	* < 0.05	8.89	1.9	> 0.05
14,15- DHET	0.39	0.1	0.36	0.7	> 0.05	0.52	0.16	> 0.05	0.49	0.04	> 0.05	0.29	0.05	> 0.05
5,6-EET	0.25	0.04	0.3	0.13	> 0.05	0.18	0.08	> 0.05	0.21	0.03	> 0.05	0.32	0.08	> 0.05
5,6-DHET	0.28	0.11	0.32	0.05	> 0.05	0.16	0.02	> 0.05	0.38	0.52	> 0.05	0.32	0.06	> 0.05
11,12- EET	0.14	0.02	n.d.	n.d.	n.d.	0.13	0.04	> 0.05	0.10	0.03	> 0.05	0.10	0.02	> 0.05
11,12- DHET	0.33	0.06	0.37	0.04	> 0.05	0.31	0.03	> 0.05	0.3	0.08	> 0.05	0.2	0.11	> 0.05
8,9-EET	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
8,9-DHET	0.15	0.02	0.24	0.7	> 0.05	0.16	0.03	> 0.05	0.28	0.11	> 0.05	0.21	0.05	> 0.05
LOX														
5-HETE	0.78	0.16	0.64	0.14	> 0.05	0.81	0.12	> 0.05	0.62	0.11	> 0.05	0.58	0.08	> 0.05
12-HETE	1.16	0.23	0.85	0.20	> 0.05	1.03	0.38	> 0.05	0.91	0.20	> 0.05	0.88	0.13	> 0.05
15-HETE	1.08	0.35	1.06	0.24	> 0.05	0.91	0.27	> 0.05	1.11	0.27	> 0.05	1.21	0.34	> 0.05
20-HETE	0.32	0.05	0.30	0.06	> 0.05	0.33	0.04	> 0.05	0.24	0.05	> 0.05	0.41	0.08	> 0.05
LTB ₄	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
COX														
PGE ₂	2.37	0.39	2.53	0.42	> 0.05	1.88	0.61	> 0.05	2.26	0.28	> 0.05	1.87	0.48	> 0.05
PGD ₂	1.36	0.41	0.86	0.16	> 0.05	1.12	0.30	> 0.05	1.83	0.67	> 0.05	1.07	0.32	> 0.05
6-keto- PGF _{1α}	18.2	2.32	15.03	1.88	> 0.05	19.4	3.38	> 0.05	20.9	1.08	> 0.05	20.16	0.91	> 0.05
PGF _{2α}	0.15	0.05	0.45	0.28	> 0.05	0.29	0.11	> 0.05	0.19	0.08	> 0.05	0.08	0.03	> 0.05
TXB ₂	0.18	0.09	0.59	0.34	> 0.05	0.33	0.14	> 0.05	0.27	0.05	> 0.05	0.37	0.12	> 0.05

Table S3: Full list of the 615 tested compounds for the CYP-inhibition repurposing screen, as well as molecular weight and indication. Each compound was tested in duplicates for the inhibition of CYP3A4 and CYP2J2. Substances considered specific for CYP2J2-inhibition are marked in green, control substances used in this study are marked in blue and nonspecific inhibitors of both CYP2J2 and CYP3A4 are marked in red.

Name	Mol. Wt.	Indication	% Inhibition I CYP3A4	% Inhibition II CYP3A4	% Inhibition I CYP2J2	% Inhibition II CYP2J2
Clindamycin HCl	461.4	Antibiotic	76.31	31.57	-8.18	-17.89
Felbamate	238.2	Anticonvulsant	53.63	20.80	-3.85	-18.25
Cyclosporine A	1202.6	Immunosuppressive; Immunomodulatory; Antirheumatic; Dermatologic Agent	89.88	81.69	46.19	34.99
Donepezil HCl	416	Parasympathomimetic; Nootropic	61.21	26.23	31.44	22.07
Lincomycin HCl	443	Antibiotic; Antibacterial	44.00	12.31	-7.22	-18.88
Mycophenolic Acid	320.3	Antibiotic; Antineoplastic	48.65	23.17	-6.95	-24.78
Sirolimus (Rapamycin)	914.2	Immunosuppressant	94.15	91.99	75.07	69.93
Spectinomycin HCl Pentahydrate	495.3	Antibiotic; Antibacterial	32.34	12.70	-7.74	-16.16
Amiodarone HCl	681.8	Antiarrhythmic	32.46	21.53	87.28	84.24
Nicardipine HCl	516	Antihypertensive; Vasodilator; Antiarrhythmic	91.83	90.09	90.57	88.73
Pimozide	461.6	Antipsychotic	84.22	59.28	78.17	80.11
Loperamide HCl	513.5	Antidiarrheal	53.41	11.19	64.53	60.28
Tolbutamide	270.3	Hypoglycemic Agent; Antidiabetic	42.16	7.05	-21.02	-46.41
Glipizide	445.5	Hypoglycemic; Antidiabetic	45.20	4.47	-18.84	-37.36
Phentolamine HCl	317.8	Vasodilator	45.72	18.47	10.54	-5.57
Quinine HCl H2O	396.9	Muscle Relaxant and antihypertensive agent	48.09	15.07	-13.73	-29.97
Propafenone HCl	377.9	Antiarrhythmic	47.90	20.80	4.75	-16.71
Phenytoin	252.3	Anticonvulsant	20.95	3.39	-4.66	-16.92
Procainamide HCl	271.8	Antiarrhythmic	9.97	0.12	-12.70	-27.94
Lidocaine HCl H2O	288.8	Anesthetic; Antiarrhythmic	3.59	-6.69	-14.59	-25.87
Flecainide Acetate	474.4	Antiarrhythmic	66.12	21.40	-12.29	-31.88
Rosiglitazone	357.4	Hypoglycemic agent	52.62	16.92	-10.62	-26.13
Amantadine HCl	187.7	Antiviral/Antiparkinsonian	41.04	2.27	-26.04	-39.31
Prazosin HCl	419.9	Antihypertensive	36.65	1.62	-8.53	-28.12
Clonidine HCl	266.6	Antihypertensive treatment	39.35	2.05	-14.63	-39.91
Guanabenz Acetate	291.1	Antihypertensive	42.84	10.85	-8.73	-24.99
Dihydroergotamine Mesylate	679.8	Antimigraine; Vasoconstrictor; Analgesic	90.37	80.44	6.69	-11.78

Emtricitabine	247.3	Antiviral	2.99	7.57	-14.35	-37.62
Betaxolol HCl	343.9	Antihypertensive	-1.77	-0.06	-11.59	-35.27
Caffeine	194.2	Central Nervous System Stimulant; Anorexigenic Agent	-7.58	-6.56	-17.74	-28.22
(S)-Timolol Maleate	432.5	Antihypertensive; Anti-Arrhythmia agent	66.49	27.13	-12.58	-36.08
Salbutamol Hemisulfate	576.7	Bronchodilator	47.19	10.41	-16.73	-46.54
Pindolol	248.3	Hypertensive; Vasodilator	45.42	4.17	-20.15	-38.74
Dobutamine HCl	337.8	Sympathomimetic; Cardiotonic	43.48	22.87	-4.50	-22.32
Sotalol HCl	308.8	Anti-Arrhythmia	35.53	-0.49	-18.08	-37.12
Maprotiline HCl	313.9	Antidepressant	50.04	29.25	11.91	-9.54
Pilocarpine HCl	244.7	Anti-glaucoma and xerostomia treatment	37.78	16.19	-13.24	-33.39
Ipratropium Br	412.4	Bronchodilator; Antispasmodic	8.73	-2.21	-14.31	-26.40
Tropicamide	284.4	Anticholinergic; Mydriatic	33.58	26.36	55.08	46.73
Pancuronium 2Br	732.7	Muscle relaxant; Neuromuscular Nondepolarizing Agent	-8.25	-9.28	-15.46	-28.77
Ivermectin	875.1	Anthelmintic; Antiprotozoal; Antinematodal	89.84	73.20	62.86	49.37
Haloperidol	375.9	Antipsychotic; Schizophrenia treatment	57.19	12.44	64.21	54.72
Cimetidine	252.3	Anti-Ulcer	47.71	3.43	-19.31	-38.90
Zonisamide	212.2	Anti-epileptic agent	37.22	6.32	-20.48	-42.68
Zoledronic Acid Monohydrate	290.1	Bone conservation agent	40.40	1.71	-14.73	-32.06
Naltrexone HCl	377.9	Narcotic antagonist used for treatment of heroin and alcohol addiction	37.55	3.78	-14.87	-34.88
Zolmitriptan	287.4	Antimigrane (acute migranes treatment)	32.01	4.34	-14.89	-42.99
Memantine HCl	215.8	Antiparkinson; Antidyskinetic Agent	23.76	2.31	-15.12	-36.65
Riluzole HCl	270.7	Anticonvulsant; Neuroprotective	12.63	-4.37	19.22	14.89
Propofol	178.3	Anaesthetic	-1.84	-16.00	-21.04	-34.43
Aminophylline	420.4	Bronchodilator	65.59	26.14	-15.00	-37.80
Nateglinide	317.4	Antidiabetic (treatment of type 2 diabetes)	50.19	5.93	-16.65	-38.82
(±) Isoproterenol HCl	247.7	Bronchodilator	46.55	14.85	-18.89	-37.12
Acetylcholine Chloride	181.7	Cholinergic	45.05	3.86	-15.76	-37.62
Atropine Sulfate Monohydrate	694.8	Antispasmodic agent	37.89	3.26	-12.92	-35.24
Apomorphine HCl Hemihydrate	321.8	Non selective dopamine agonist and anti - Parkinsonian	68.55	45.66	38.15	41.96
Chlorpromazine HCl	355.3	Antipsychotic	58.17	28.68	24.79	4.35
Fluphenazine HCl	510.4	Antipsychotic	48.84	46.65	44.13	22.51
Risperidone	410.5	Antipsychotic	6.85	-0.40	4.57	-17.50
Diphenhydramine HCl	291.8	Antiallergy; antitussive; antiemetic and sedative	-20.55	-8.07	-14.51	-25.33
Promethazine HCl	320.9	Anti-Allergic; Sedative	76.09	36.48	19.23	4.53
Ranitidine HCl	350.9	Antiulcer	44.64	5.16	-13.40	-38.90

Epinephrine (L-(-)-Epinephrine-(+)-Bitartrate)	333.3	Vasoconstrictor; Mydriatic; Bronchodilator	43.59	8.60	-14.98	-40.44
Norepinephrine Bitartrate Monohydrate	337.3	Vasoconstrictor	38.79	1.06	-10.96	-43.26
Quetiapine Fumarate	883.1	Antipsychotic	56.59	25.93	60.98	61.32
Imipramine HCl	316.9	Antidepressant	44.11	14.42	4.29	-18.23
Amoxapine	313.8	Antidepressant	51.23	24.42	20.05	-3.98
Metoclopramide HCl	336.3	Antipsychotic and antiemetic agent	13.34	-4.24	-11.29	-29.76
Nalbuphine HCl Dihydrate	429.9	Narcotic; Analgesic; Opioid	-0.42	-13.85	-14.27	-26.50
Carbachol (Carbamylcholine) Chloride	182.7	Glaucoma treatment; Cholinergic Agonist	-6.56	-9.84	-14.21	-25.48
Famotidine	337.5	Ant ulcerative	66.12	28.21	-6.09	-21.91
Isoniazid	137.1	Antitubercular Agent	55.47	19.38	-14.13	-30.18
Ticlopidine HCl	300.2	Platelet Aggregation Inhibitor; Fibrinolytic	54.35	23.30	9.33	4.17
Clemastine Fumarate	460	Antipruritic; Anti-Allergic; Antihistamine	68.10	38.21	30.65	11.21
Vardenafil	488.6	Erectile dysfunction and impotence	63.79	31.87	45.44	23.79
Linezolid	337.4	Antibiotic; Antibacterial	37.29	-28.02	-4.68	-18.83
Docetaxel (Taxotere)	807.9	Antineoplastic	94.23	93.15	49.44	34.39
Olopatadine	337.4	Antihistamine agent	13.34	-1.09	-5.54	-20.44
Tolcapone	273.2	Antiparkinson; Antidyskinetic	46.36	29.29	40.24	49.00
Olmesartan	446.5	Antihypertensive agent	18.77	12.53	-5.95	-17.37
Nisoldipine	388.4	Antihypertensive; Vasodilator	79.91	65.23	86.09	87.29
Olanzapine	312.4	Antipsychotic; Antiemetic	54.87	19.89	-5.97	-18.23
Lovastatin	404.5	Anticholesteremic	88.27	71.69	69.71	67.35
Lamotrigine	256.1	Antidepressant; Anticonvulsant	48.20	18.21	-3.43	-20.16
Azathioprine	277.3	Immunosuppressant	45.76	20.11	-1.80	-17.68
Sildenafil Citrate	666.7	Erectile dysfunction; vasodilator; pulmonary arterial hypertension treatment	54.98	34.55	4.33	-8.00
Atovaquone	366.8	Antipneumocystic/Antimalarial	36.28	13.69	-1.11	-5.05
Sertaconazole	437.8	Used to treat skin infections (fungal)	97.30	97.20	97.86	97.00
Cefepime HCl Hydrate	571.5	Antibiotic	18.51	13.13	-6.33	-8.39
Aripiprazole	448.4	Antipsychotic	18.77	12.14	94.22	91.44
Candesartan	440.5	Antihypertensive agent	54.61	14.55	-15.14	-35.32
Butenafine HCl	353.9	Antifungal	62.07	31.79	67.88	65.37
Dorzolamide HCl	360.9	Antihypertensive	39.76	8.65	-19.57	-40.57
Escitalopram	324.4	Antidepressant	43.63	8.09	-15.52	-32.40
Eprosartan Mesylate	520.6	Antihypertensive	39.02	6.67	-18.36	-41.79
Entacapone	305.3	Antiparkinsonian	40.78	16.92	49.35	43.99
Bleomycin Sulfate	1512.6	Antineoplastic	26.27	0.59	-11.61	-30.34
Guanfacine HCl	282.6	Antihypertensive	41.53	22.91	-11.39	-24.59
Tizanidine HCl	290.2	Muscle relaxant	6.40	1.67	-14.31	-31.67

Carvedilol	406.5	Antihypertensive; Congestive heart failure treatment	66.49	64.06	46.33	30.08
Flumazenil	303.3	Benzodiazepine antagonist	50.93	-2.99	-17.07	-35.40
Gefitinib	446.9	Antineoplastic	54.53	22.48	77.15	70.80
Imatinib Mesylate	589.7	Antineoplastic	66.45	37.04	94.98	94.31
Idarubicin HCl	534	Antineoplastic; Antibiotic	50.71	32.86	53.77	47.18
Montelukast Na	608.2	Anti-Asthmatic; Antiarrhythmic	92.65	86.90	95.12	94.57
Exemestane	296.4	Antineoplastic	-2.29	-53.88	42.48	21.29
Dinoprostone	352.5	Muscle relaxant (used in labor); bone resorption stimulant	21.40	1.97	-10.60	-29.97
Metformin HCl	165.6	Antidiabetic	7.53	-3.07	-15.88	-35.24
Anagrelide	256.1	Used in treating thrombocytosis	0.93	-9.88	-19.01	-32.82
Dofetilide	441.6	Antiarrhythmic	-5.14	-8.55	-15.10	-27.10
Erlotinib	393.4	Can be used in treating several types of non-small cell cancer (eg. Lung)	70.88	45.23	83.66	80.32
Tacrine HCl	234.7	Alzheimer's disease treatment	43.14	1.84	-15.52	-41.09
Galantamine HBr	368.3	Alzheimer's disease treatment	44.90	8.56	-14.89	-37.17
Amloride HCl 2H2O	302.1	Diuretic	35.27	8.86	-15.42	-37.44
Amlodipine	408.9	Antihypertensive agent and in treating angina pectoris	83.51	70.44	55.80	45.06
Diltiazem HCl	451	Antihypertensive; Vasodilator; Cardiovascular Agent (antianginal); Antiarrhythmic	60.08	34.46	-14.07	-33.83
Nifedipine	346.3	Antihypertensive; Vasodilator; Tocolytic	59.44	53.29	86.88	81.76
Nimodipine	418.4	Antihypertensive; Vasodilator	81.41	78.80	72.85	63.64
Verapamil HCl	491.1	Antihypertensive; Antiangina; Antiarrhythmia; and most recently; cluster headaches treatment	32.91	20.45	13.82	9.20
Gabapentin	171.2	Anticonvulsant; Anti-anxiety Agent; Antiparkinson Agent; Analgesic	-7.69	-12.25	-14.23	-23.11
Felodipine	384.3	Antihypertensive	93.63	91.38	93.17	90.24
Phenoxybenzamine HCl	340.3	Antihypertensive; Vasodilator	53.75	-17.90	74.53	75.39
Trifluoperazine HCl	480.4	Antipsychotic; Antiemetics	76.84	55.57	53.87	42.43
Latanoprost	432.6	Antiglaucoma; Antihypertensive; Neuroprotective	65.89	39.46	37.04	35.56
Alfuzosin	389.5	Used in treating benign prostatic hyperplasia (BPH). It works by relaxing the muscles	33.62	9.60	-11.73	-38.90
Bromocriptine Mesylate	750.7	Antiparkinson; Antidyskinetic	93.52	88.02	86.30	83.92
Clozapine	326.8	Antipsychotic	40.03	11.49	2.11	-15.30
Acitretin	326.4	Dermatologic	39.05	30.84	61.00	55.24
Calcitriol	416.6	Antihypocalcemic Agent; Antihypoparathyroid Agent; Vitamin (Vitamin D); Bone Density Conservation Agent	83.99	83.32	96.31	94.65
Ketoconazole	531.4	Antifungal	97.04	97.11	97.10	96.19

Cromolyn Na (Disodium Cromoglycate)	512.3	Mast cell stabilizer; Antiallergy; Antiasthma	51.23	0.46	-11.65	-40.07
Capsaicin	305.4	Analgesic	86.62	71.60	87.83	88.07
Dexamethasone	392.5	Anti-inflammatory; Hormonal; Antineoplastic	54.95	9.81	-4.88	-23.50
Dipyridamole	504.6	Vasodilator; Platelet aggregation Inhibitor	78.52	64.11	75.67	71.40
Ethacrynic Acid	303.1	Diuretic	41.45	4.86	-3.00	-24.57
Indomethacin	357.8	Non-steroidal antiinflammatory; Analgesic; Antipyretic	36.99	5.67	-8.79	-33.70
Naproxen	230.3	Analgesic; anti-inflammatory; antipyretic	29.83	0.93	-9.11	-30.81
Ibuprofen	206.3	Nonsteroidal anti-inflammatory; Analgesic;	12.63	-8.76	-12.42	-31.17
Bumetanide	364.4	Diuretic	-8.78	-15.35	-16.81	-36.05
Neomycin Sulfate	908.9	Antibiotic	-13.39	-9.71	-12.38	-20.73
Auranofin	678.5	Antirheumatic	96.85	95.69	44.32	30.63
Captopril	217.3	Antihypertensive	43.36	6.49	-17.58	-42.39
Tranlycypromine Hemisulfate	364.5	Antidepressant and anxiolytic	45.80	4.42	-11.67	-35.01
Piroxicam	331.3	Non-steroidal anti-inflammatory agent	38.90	3.86	-10.34	-36.60
Moxifloxacin HCl	437.9	Antibiotic	39.09	2.31	-6.67	-32.37
Carbidopa	226.2	Antiparkinson; Antidyskinetic agent	45.91	5.98	-4.39	-18.51
Ketoprofen	254.3	Nonsteroidal anti-inflammatory; Analgesic; Antipyretic	1.23	2.01	-11.19	-31.01
Meloxicam	351.4	Nonsteroidal Anti-inflammatory; Analgesic; Antineoplastic	4.12	-3.29	-12.96	-34.62
Terbinafine HCl	327.9	Antifungal	50.15	-6.13	62.33	60.75
Sodium Phenylbutyrate	186.2	Antineoplastic	-5.55	-12.17	-14.25	-20.44
Simvastatin	418.6	Anticholesteremic; antilipemic	92.58	85.48	90.14	88.91
Goserelin Acetate	1329.5	Antineoplastic	58.51	26.14	-8.30	-26.63
Raloxifene HCl	510.1	Antihypocalcemic; Osteoporosis Prophylactic; Bone Density Conservation Agent	94.86	91.77	75.01	71.21
Rifampin (Rifampicin)	822.9	Antibiotic; Antituberculosis Agent; Leprostatic	56.56	22.57	15.80	3.46
Etoposide	588.6	Antineoplastic	41.41	10.93	-6.11	-25.19
Mitomycin C	334.3	Antineoplastic antibiotic; Alkylating Agent; Cross-Linking Reagent	34.70	12.53	7.66	-10.48
Delavirdine Mesylate	552.7	Antiviral; Anti-HIV Agent	81.97	74.79	95.38	94.34
Daunorubicin HCl	564	Antineoplastic	21.47	15.41	47.36	41.83
Doxorubicin HCl	580	Antineoplastic	32.76	34.93	42.16	34.65
Cetirizine HCl	461.8	Anti-Allergic; Antihistamine	-0.98	-5.10	-6.15	-14.55
Lapatinib Ditosylate	925.5	Antineoplastic	50.82	45.32	92.66	91.62
Pioglitazone HCl	392.9	Antidiabetic; Hypoglycemic Agent	-10.69	-20.09	10.06	-1.13
Rivastigmine Tartrate	400.4	Neuroprotective; Dementia treatment	-25.23	-20.65	-16.57	-44.79
Ergotamine Tartrate	1313.4	Vasoconstrictor	66.45	61.52	32.08	10.35

Sulindac	356.4	Nonsteroidal anti-inflammatory; Analgesic; Antipyretic; Antineoplastic	-10.28	-12.51	36.96	26.58
Valproic Acid	144.2	Anticonvulsant and mood-stabilizer; Also used to treat migraine headaches and schizophrenia.	-18.41	-19.02	-13.56	-37.04
Calcipotriene	412.6	Dermatologic Agent; Antipsoriatic	48.35	55.27	91.54	87.03
Zafirlukast	575.7	Antiasthmatic	62.18	66.52	89.20	86.72
Zileuton	236.3	Antiasthmatic	-11.85	-21.26	-11.81	-22.06
Bortezomib	384.2	Antineoplastic	16.19	13.60	-16.39	-25.82
Diazoxide	230.7	Antihypertensive; Vasodilator; Diuretic	-30.07	-32.72	-19.05	-49.28
Glyburide	494	Hypoglycemic; Antidiabetic	-3.23	-13.54	12.13	1.16
Minoxidil	209.2	Antihypertensive; Vasodilator	-36.06	-33.06	-20.66	-47.04
Tolazamide	311.4	Hypoglycemic Agent; Antidiabetic	-12.52	-15.66	-3.15	-23.47
Bexarotene	348.5	Antineoplastic	30.02	31.79	-10.76	-48.27
Tranexamic Acid	157.2	Antifibrinolytic	-29.13	-31.81	-18.84	-40.65
Celecoxib	381.4	Non-steroidal anti-inflammatory; Anti-osteoarthritis; Anti-rheumatoid; analgesic	0.67	-14.28	55.02	47.70
Levetiracetam	170.2	Anticonvulsant; Nootropic	-27.40	-23.15	-17.43	-34.75
Letrozole	285.3	Antineoplastic	-8.14	-1.61	-14.15	-34.15
Anastrozole	293.4	Antineoplastic	16.71	12.22	-1.25	-12.07
Bicalutamide	430.4	Antineoplastic	41.68	37.04	83.70	79.17
Clindamycin Palmitate HCl	699.9	Antibiotic	23.01	30.11	52.58	40.89
Vorinostat	264.3	Antineoplastic; Treatment of cutaneous T cell lymphoma (CTCL)	-27.22	-31.77	-4.48	-37.17
Didanosine	236.2	Antiviral; Anti-HIV Agent	-33.29	-29.10	-18.82	-44.98
Dolasetron	324.4	Antinauseant and antiemetic agent.	-25.72	-34.66	-14.09	-37.70
Enalaprilat Maleate	492.5	Antihypertensive	-32.20	-25.18	-20.42	-41.35
Fluvastatin Na	433.5	Anticholesteremic	-18.30	-27.46	-3.83	-22.82
Fosinopril Na	585.6	Antihypertensive	-16.91	-15.96	12.17	-4.71
Gemcitabine HCl	299.7	Antineoplastic; Antiviral; Immunosuppressive	4.42	-22.85	-14.75	-35.11
Granisetron HCl	348.9	Antiemetic	-11.70	-14.02	-11.85	-28.04
Oxaliplatin	397.3	Antineoplastic	-24.29	-29.44	-12.36	-45.21
Atazanavir	704.9	Antiretroviral drug and protease inhibitor	75.56	75.61	69.93	56.83
Mycophenolate Mofetil	433.5	Antineoplastic; Immunosuppressant	13.00	5.42	0.06	-19.01
Clofarabine	303.7	Antineoplastic	-32.28	-37.37	-16.00	-43.72
Cabergoline	451.6	Antiparkinson	5.17	-9.62	-14.94	-35.92
Ibandronate Na Monohydrate	359.2	Inhibits osteoclast-mediated bone resorption	-26.58	-24.27	-15.72	-40.18
Imipenem	299.4	inhibits osteoclast-mediated bone resorption	-20.10	-30.82	-11.01	-35.90
Lomustine	233.7	Antineoplastic	-18.56	-26.21	-9.98	-27.78
Adapalene	412.5	Dermatologic	72.82	73.93	53.10	49.79

Meropenem	383.5	Antibiotic; Antibacterial	-22.72	-19.88	-16.63	-29.48
Oseltamivir Phosphate	410.4	Antiviral	-29.43	-33.32	-7.74	-49.10
Pamidronate Disodium Pentahydrate (Pamidronic Acid)	369.1	Promotes osteoblast proliferation and differentiation while inhibiting osteoclastogenesis and osteoclast function.	-34.34	-43.10	-15.76	-51.95
Pramipexole Dihydrochloride Monohydrate	302.3	Nonergot dopamine agonist	-29.62	-35.00	-13.02	-45.42
Triptorelin Acetate	1371.5	Causes a surge in the testosterone level. Used in prostate cancer patients.	66.68	65.53	-13.32	-47.85
Risredonic Acid	283.1	Used to strengthen bone; treat or prevent osteoporosis	-26.17	-29.53	-13.95	-52.10
Rocuronium Bromide	609.7	Muscle Relaxant	-2.70	-10.23	-19.69	-47.01
Vinorelbine	778.9	Antineoplastic for treatment breast and non-small cell lung cancer.	-9.34	-0.53	-14.39	-46.28
Salmeterol	415.6	Can be used for the treatment of asthma and chronic obstructive pulmonary disease(COPD).	29.46	31.57	43.83	13.27
Vincristine Sulfate	923	Antineoplastic	-7.24	-14.45	-25.13	-48.19
Aspirin (Acetylsalicylic Acid)	180.2	Analgesic	-13.27	-20.96	-16.29	-34.96
Acyclovir (Acycloguanosine) Zovirax	225.2	Antiviral	-31.04	-43.45	-13.73	-49.26
Zidovudine (3'-Azido-3'-Deoxythymidine)	267.2	Antiviral; Anti-HIV	-29.20	-36.43	-12.17	-47.59
Allopurinol	136.1	Antiurolithic	-28.53	-35.35	-14.65	-49.13
Altretamine	210.3	Antineoplastic	-27.25	-35.95	-12.46	-45.55
Alendronate Na Trihydrate	325.1	Bone resorption inhibitor	-27.22	-35.48	-13.65	-47.77
Albendazole	265.3	Anthelminthic	-27.22	-22.77	34.36	8.94
Sumatriptan Succinate	413.5	Antimigraine; Vasoconstrictor	-26.99	-27.07	-14.79	-38.58
Amifostine	214.2	Antineoplastic	-23.17	-29.96	-12.03	-37.44
4-Aminosalicylic Acid	153.1	Antibacterial	-19.23	-16.60	-13.89	-39.39
Mesalamine (5-Aminosalicylic Acid)	153.1	Anti-inflammatory	-10.99	-13.50	-6.85	-24.15
Ampicillin Trihydrate	403.5	Broad-spectrum antibiotic; Anti-Bacterial	-30.44	-33.15	-9.11	-44.38
(±)-Atenolol	266.3	Antihypertensive	-38.80	-32.37	-12.96	-48.63
Atracurium Besylate	1243.5	Neuromuscular blocking agent	30.21	20.67	-0.79	-24.52
Vinblastine Sulfate	909.1	Antineoplastic	8.77	9.47	-14.89	-57.64
Azithromycin	749	Antibiotic	-28.19	-37.76	-10.99	-46.99
Aztreonam	435.4	Antibiotic	-22.12	-35.22	-11.13	-38.61
Betamethasone	392.5	Anti-inflammatory; Immunosuppressive	-17.85	-23.50	-6.69	-27.60
Bisacodyl	361.4	Laxative	-9.68	-16.52	17.11	6.36
Buspirone HCl	422	Anti-anxiety Agent; Anxiolytic; Sedative	-5.40	-8.63	-6.69	-16.69
Carboplatin	339.2	Antineoplastic	-15.56	-19.75	-15.72	-24.10
Carbamazepine	236.3	Anticonvulsant; Antimanic	-20.85	-26.13	0.50	-18.20
Cefotaxime Acid	455.5	Broad-spectrum antibiotic; Anti-Bacterial	-20.88	-23.02	-5.22	-24.83

Ceftazidime	546.6	Antibiotic	-24.52	-22.16	-11.29	-26.53
Chloramphenicol	323.1	Broad-spectrum antibiotic; Anti-Bacterial. A tetracycline.	-14.74	-19.40	-4.37	-27.18
Chlorambucil	304.2	Antineoplastic; alkylating agent	-17.36	-23.50	-1.77	-21.54
Chlorpheniramine Maleate	390.9	Antipruritic; Anti-Allergic; Antihistamine	-15.11	-15.18	-1.33	-18.64
Chloroquine Diphosphate	515.9	Antimalarial	-15.04	-16.13	1.63	-15.07
Thalidomide	258.2	Immunosuppressant; Leprostatic; Angiogenesis Inhibitor	-17.47	-6.86	-1.45	-11.62
Ciprofloxacin	331.3	Antibiotic	-13.16	-7.04	1.71	-12.93
Citalopram HBr	405.3	Antidepressant	-5.33	-9.80	-1.53	-10.89
Clarithromycin	748	Antibiotic	-4.05	-3.59	-10.78	-38.37
Clomiphene Citrate	598.1	Estrogen Modulator; Fertility Agent	52.58	53.51	86.24	85.75
Clopidogrel Hydrogen Sulfate	419.9	Antiplatelet Agent; Platelet Aggregation Inhibitor; Fibrinolytic	11.43	3.13	54.67	53.02
Clobetasol Propionate	467	Anti-inflammatory; Corticosteroid	-1.02	-7.60	80.15	76.30
Orphenadrine Citrate	461.5	Muscle relaxant; Antiparkinson agent	-14.40	-16.47	-8.04	-35.56
Crotamiton	203.3	Scabicial (for treating scabies) and antipruritic	-25.49	-28.50	-9.27	-22.01
Cyclophosphamide monohydrate	279.1	Antineoplastic; Immunosuppressive	-14.81	-22.16	-16.53	-29.48
Cytarabine	243.2	Antineoplastic; Antiviral; Immunosuppressive	-10.20	-16.86	-12.94	-30.00
Dacarbazine	182.2	Antineoplastic	-10.80	-11.30	-11.77	-25.72
Danazol	337.5	Estrogen Antagonist; Endometriosis treatment	90.40	90.78	98.41	97.81
Desloratadine	310.8	Antihistamine; Antiallergy	13.75	8.39	36.09	16.93
Dextromethorphan	271.4	An Antitussive drug (cough suppressant)	-27.67	-26.64	-17.07	-45.68
Diclofenac Na Salt	318.1	Non-steroidal anti-inflammatory	-23.43	-33.28	-19.71	-50.01
Zalcitabine	211.2	Antiviral; Anti-HIV Agent	-28.60	-33.11	-26.30	-43.57
Diffunisal	250.2	Nonsteroidal Anti-inflammatory; Analgesic; Antipyretic	-24.56	-38.71	-18.93	-42.47
Disulfiram	296.5	Alcohol Deterrent	81.15	85.39	97.12	96.58
Doxazosin Mesylate	547.6	Antihypertensive; Vasodilator	-41.91	-44.66	74.39	72.96
Doxycycline Monohydrate	462.4	Broad-spectrum antibiotic synthetically derived from oxytetracycline.	-18.03	-20.61	-15.70	-30.86
Enalapril	376.4	Used in reducing hypertension and in treatment of chronic heart failure.	-12.15	-16.99	-16.65	-34.96
Esomeprazole Potassium	383.5	An antiulcerative agent.	12.40	6.84	17.65	9.54
Estradiol	272.4	Estrogen; Hormonal replacement; Antineoplastic	13.53	10.59	84.66	84.13
Estrone	270.4	Antineoplastic; Estrogen	10.94	16.27	22.79	-0.14
Etidronate Disodium	250	Antiosteoporotic	-26.28	-40.60	-21.67	-44.79
Famciclovir	321.3	Antiviral	-30.82	-26.77	-20.05	-44.69
Fenoldopam Mesylate	401.9	Antihypertensive	-17.06	-22.77	-20.82	-44.06
Fenoprofen Calcium	558.6	Analgesic	-25.23	-26.17	-15.58	-31.35
Fenofibrate	360.8	Antilipidemic	-28.34	-24.01	80.11	75.86

Finasteride	372.5	Benign prostatic hypertrophy treatment	12.66	-3.29	-11.11	-26.16
Fluorouracil (5-Fluorouracil)	130.1	Antineoplastic	-12.19	-24.40	-17.94	-33.96
Flurbiprofen	244.3	Nonsteroidal anti-inflammatory agent; Antipyretic; Analgesic	-8.70	-18.84	-7.05	-14.16
Amitriptyline HCl	313.9	Antidepressant	-15.67	-19.96	-0.32	-26.84
Floxuridine	246.2	Antineoplastic	-27.63	-37.07	-20.32	-49.21
Fluocinolone Acetonide	452.5	Antiinflammatory	-8.03	-13.67	33.88	18.57
Flutamide	276.2	Antineoplastic; Hormonal	-20.85	-19.66	-2.16	-32.63
Fluconazole	306.3	Antifungal	18.14	17.40	-13.89	-38.45
Furosemide	330.7	Diuretic	-24.41	-36.73	-19.67	-41.72
Ganciclovir	255.2	Antiviral	-25.98	-25.78	-12.80	-37.41
Gatifloxacin	375.4	Antibiotic	-18.90	-19.66	-14.45	-33.86
Gentamycin Sulfate	575.7	Antibiotic; Antibacterial	-13.84	-9.88	-3.65	-18.41
Gemfibrozil	250.3	Antilipemic	-23.69	-18.03	-14.75	-23.47
Glimepiride	490.6	Hypoglycemic; Antidiabetic	-24.07	-32.12	15.27	-8.39
Hydrocortisone	362.5	Anti-inflammatory	-30.03	-39.10	-13.42	-45.89
Hydrocortisone Acetate	404.5	Anti-inflammatory	-34.15	-39.10	-1.43	-30.21
Idoxuridine	354.1	Antiviral	-24.03	-31.51	-14.53	-35.40
Ifosfamide	261.1	Antineoplastic; Immunosuppressive	-33.40	-26.86	-13.58	-47.01
Imiquimod	240.3	Immunomodulant; Antineoplastic; Antiviral; Adjuvant	-21.00	-24.66	-7.40	-39.99
Indapamide	365.8	Antihypertensive; Diuretic	-22.79	-33.19	-5.91	-24.10
Itraconazole	705.6	Antifungal	86.17	83.41	85.37	79.43
Levonorgestrel	312.4	Contraceptive	8.43	1.75	67.82	60.25
Levofloxacin HCl	397.8	Broad spectrum antibiotic.	-14.51	-13.11	-7.74	-23.60
Leflunomide	270.2	Antirheumatic; Antineoplastic; Anti-inflammatory	-12.15	-16.47	10.98	-16.30
Lisinopril 2H2O	441.5	Antihypertensive	-32.35	-32.46	-14.25	-55.76
Loratadine	382.9	Anti-Allergic; Antihistamine	-18.56	-28.41	8.33	7.82
Losartan Potassium	461	Antihypertensive; Antiarrhythmic	-20.96	-21.90	-10.84	-37.96
Mebendazole	295.3	Anthelmintic	-32.32	-41.42	53.16	41.51
Medroxyprogesterone Acetate	386.5	Contraceptive	-33.36	-35.61	1.69	-14.55
Mefenamic Acid	241.3	Non-steroidal anti-inflammatory; Analgesic; Antipyretic	-23.28	-25.70	-12.98	-37.80
Melphalan	305.2	A chemotherapy drug. Can be used as treatment for ovarian cancer and multiple myeloma.	30.06	18.95	21.52	8.45
Methyldopa Sesquihydrate (L-?-Methyl-Dopa Sesquihydrate)	229.2	An antihypertensive agent	-20.62	-27.81	-16.35	-27.86
Methylprednisolone	374.5	Anti-inflammatory; Antiemetic; Neuroprotective	-3.98	-28.93	12.51	15.88
Metoprolol Tartrate	684.8	Antihypertensive; Antiarrhythmic	-40.41	-31.56	-9.72	-42.21

Methimazole	114.2	Antithyroid Agent	-28.94	-40.13	-13.48	-46.70
Metronidazole	171.2	Anti-Infective; Antiprotozoal	-27.89	-30.09	-13.22	-44.66
Minocycline	457.5	Broad spectrum antibiotic. Tetracycline antibiotic usually used to treat acne vulgaris.	-30.55	-32.72	-14.37	-41.79
Mitoxantrone HCl	517.4	Antineoplastic	-1.95	-6.91	7.39	-20.86
Paclitaxel (Taxol)	853.9	Antineoplastic	-5.18	-11.86	-15.43	-39.31
Nabumetone	228.3	Nonsteroidal anti-inflammatory; Antineoplastic	-17.62	-16.95	18.36	2.68
Naphazoline HCl	246.7	Vasoconstrictor; ocular agent	-21.41	-17.03	-10.72	-29.01
Nefazodone HCl	506.5	Antidepressant	56.67	55.79	81.52	80.01
Norethindrone	298.4	Contraceptives	21.44	14.34	45.49	43.05
Norfloxacin	319.3	Antibiotic	-19.50	-19.84	-2.36	-23.13
Nystatin	926.1	Antifungal; antibacterial	-7.31	-10.61	11.69	-7.06
Ofloxacin	361.4	Antibiotic	-20.81	-24.70	-4.41	-21.93
Omeprazole	345.4	Anti-Ulcer Agent	9.25	-1.91	32.20	20.32
Oxcarbazepine	252.3	Anticonvulsant	-3.64	-16.60	-1.27	-19.11
Oxiconazole Nitrate	492.2	Antifungal	97.23	97.29	97.32	96.58
Oxacillin sodium salt monohydrate	441.4	Antibiotic	-1.09	-13.54	-7.90	-13.61
Pantoprazole	383.4	Treats gastroesophageal reflux disease (GERD) and damage to the esophagus.	1.42	-2.94	25.63	23.04
Paroxetine HCl	365.8	Antidepressant	28.82	35.67	74.89	65.89
Penciclovir	253.3	An Antiviral drug used for the treatment for various herpesvirus infections	-3.34	-10.74	1.33	-6.74
Pentoxifylline	278.3	Hematologic Agent; Platelet Aggregation Inhibitor; Free Radical Scavenger	31.56	41.52	-20.15	22.12
Penicillin V Potassium	388.5	Antibiotic	31.12	24.18	-26.62	14.69
Piperacillin	517.6	An extended spectrum beta-lactam antibiotic	23.62	27.37	-21.39	10.58
Prednisolone	360.4	Antineoplastic; Hormonal; Anti-inflammatory	21.43	17.02	-20.48	14.52
Progesterone	314.5	Contraceptive	26.28	25.46	32.99	52.17
Procarbazine HCl	257.8	Antineoplastic	25.96	19.07	-5.13	31.01
Prednisone	358.4	Antineoplastic; Hormonal; Anti-inflammatory	29.69	37.78	-11.63	6.53
Primaquine Phosphate	455.3	Antimalarial; Antiprotozoal	32.99	35.95	34.20	51.29
Praziquantel	312.4	Anthelmintic	-2.43	9.77	-0.15	9.61
Quinapril HCl	475	Antihypertensive	7.10	20.08	25.83	31.89
Ranolazine 2HCl	500.5	An antianginal agent. In the United States it was used to treat chronic angina pectoris.	11.15	13.32	-14.64	25.46
Ramipril	416.5	Antihypertensive	17.38	5.11	-42.27	-6.73
Ribavirin	244.2	Antiviral	11.07	7.58	-44.31	-8.90
Nelfinavir Mesylate	663.9	Antiviral	82.13	80.89	89.61	94.48
Rimantadine HCl	215.8	Antiviral	11.91	4.70	-31.02	-0.10
Propranolol HCl	295.8	Antihypertensive; Anti-anxiety; Antiarrhythmic	17.03	12.55	-32.18	-1.63

Scopolamine HBr	384.3	A tropane alkaloid drug with muscarinic antagonist effects. It contains anticholinergic properties.	7.02	6.53	-28.44	-6.88
Spirolactone	416.6	Diuretic	-25.41	-12.31	0.38	4.98
Streptomycin Sulfate	679.7	Antibiotic	0.87	11.36	-25.74	-20.70
Sulfadiazine	250.3	Anti-Infective; Antiprotozoal	3.65	-1.64	-20.48	-17.30
Sulfasalazine	398.4	Antirheumatic; Anti-Infective	20.20	19.44	-36.88	0.49
Tamsulosin HCl	445	Antineoplastic; Symptomatic treatment of benign prostatic hyperplasia (BPH)	16.83	15.10	-37.92	-4.53
Telmisartan	514.6	Antihypertensive	10.60	4.52	87.51	91.46
Terazosin HCl	423.9	It is used for treatment of symptoms of an enlarged prostate (BPH).	21.19	12.73	-27.15	6.03
Tetracycline	444.4	A broad-spectrum polyketide antibiotic used against many bacterial infections	10.67	4.20	-17.17	1.72
Temozolomide	194.2	Antineoplastic; alkylating agent	3.09	5.66	-35.06	-11.60
Tinidazole	247.3	Antiprotozoal	2.38	4.20	-30.01	-14.98
Tobramycin	467.5	Antibiotic	-7.98	1.01	-28.34	-21.79
Topotecan HCl	457.9	Antineoplastic; Treatment of cervix; ovarian and small cell lung cancer	-9.77	-8.30	-23.89	-26.48
Toremifene Base	406	Induces estrogen -sensitive breast cancer cells to undergo apoptosis.	56.61	54.97	66.61	71.95
Tolmetin sodium dihydrate	315.3	Non-steroidal anti-inflammatory agent	20.88	16.79	-30.77	4.42
Amoxicillin	365.4	Antibiotic	11.35	5.93	-44.95	-10.43
Tramadol HCl	299.8	Analgesic; Opioid	12.70	-1.82	-37.87	-7.20
Trimethoprim	290.3	Antibiotic; Bacteriostatic; Mainly used in the prophylaxis and treatment of urinary tract infections.	5.95	7.30	-38.60	-10.05
Valacyclovir HCl	360.8	Antiviral; used in the management of herpes simplex and herpes zoster (shingles).	17.11	5.57	-36.78	-12.57
Vecuronium Bromide	637.7	Muscle relaxant	1.74	5.11	-30.44	-10.55
Venlafaxine HCl	313.9	Antidepressant	0.31	7.58	-34.56	-15.77
Bupivacaine HCl	324.9	Anesthetic; Local	0.03	-4.10	-21.51	-26.45
Ketotifen Fumarate	425.5	Antihistamine	-5.09	-14.82	-9.94	-4.21
Naloxone HCl	363.8	Narcotic antagonist	-11.00	-16.24	-15.37	-20.67
Fluoxetine HCl	345.8	Used for the treatment of major depression (including pediatric depression); obsessive-compulsive disorder; bulimia nervosa; panic disorder and premenstrual dysphoric disorder.	40.49	39.42	-26.77	11.35
Ondansetron	293.4	Used to treat nausea and vomiting in patients undergoing chemotherapy	15.28	1.92	-30.41	3.42
Tiotropium Bromide	472.4	Bronchodilator	14.68	1.55	-46.82	-13.10
Thioridazine HCl	407	Antipsychotic	60.54	47.99	89.38	95.25

Amrinone	187.2	Increases the contractions initiated in the heart and can be used with patients that have congestive heart failure.	19.21	14.87	12.23	28.81
Milrinone	211.2	Used in patients suffering from heart failure. A vasodilator.	7.66	5.20	-37.82	-10.49
Alprostadil	354.5	Vasodilator	-2.63	8.53	-30.49	-14.54
Misoprostol	382.5	Anti-Ulcer Agent; Abortifacient Agent	31.91	47.13	46.92	50.58
Argatroban	508.6	Anticoagulant	6.47	8.99	1.92	17.63
Cilastatin Na	380.4	Antibiotic adjuvant	-10.21	-4.65	-25.53	-22.34
Butoconazole Nitrate	474.8	Antifungal	97.82	97.90	96.81	97.18
Mifepristone	429.6	Contraceptive	67.80	64.28	81.60	88.09
Megestrol Acetate	384.5	Contraceptive; Hormonal; Antineoplastic	-16.48	-27.69	14.94	36.23
Tamoxifen Citrate	563.6	Antineoplastic	73.24	66.15	70.05	86.15
Aprepitant	534.4	Antiemetic	92.93	92.15	90.93	91.40
Bosentan	551.6	Antihypertensive	15.88	8.40	-29.38	-6.17
Efavirenz	315.7	Antiviral	44.74	38.37	64.36	73.15
Miglustat (N-Butyldeoxynojirimycin HCl)	255.7	Contains broad spectrum antiviral activity. Primarily used to treat Type 1 Gaucher disease (GD1).	-10.92	-6.34	-20.86	-14.86
Fulvestrant	606.8	Antineoplastic; Hormonal	64.83	63.96	71.13	72.88
Esmolol	295.4	Treatment for heart rhythm disorders.	57.12	-7.71	-19.82	-24.72
Capecitabine	359.4	Antineoplastic	15.99	15.79	-30.87	2.25
Succinylcholine Chloride 2H2O	397.3	A neuromuscular blocking agent.	10.08	1.46	-40.55	-10.87
Cyproheptadine HCl Sesquihydrate	377.9	Antihistamine; Anti-Allergic; Antipruritic	21.23	6.07	-9.03	24.67
Abacavir Sulfate	384.4	Antiviral	34.14	33.58	-19.77	19.12
Acamprosate	400.5	Alcohol Deterrent	26.51	20.90	-26.47	14.78
Acarbose	645.6	Anti-diabetic	17.03	22.54	-26.97	9.35
Acebutolol HCl	372.9	Antihypertensive	26.44	21.40	-22.95	13.22
Acetaminophen	151.2	Analgesic	23.46	22.72	-15.42	8.91
Acetazolamide	222.3	Antiglaucoma/Edema	20.16	22.58	-13.63	6.18
Acetohexamide	324.4	Antidiabetic (Hypoglycemic agent)	17.15	20.94	-15.12	2.66
Acetohydroxamic Acid	75.1	Antiurolithic	10.28	20.44	-7.46	-5.88
Acetylcysteine	163.2	Expectorant	7.74	19.03	-10.85	-10.75
Acrivastine	348.4	Antihistaminic	10.44	8.58	0.18	-4.77
Adefovir Dipivoxil	501.5	Antiviral	59.19	54.56	-34.68	3.80
Adenosine	267.2	Antiarrhythmic	7.66	13.55	-51.19	-5.82
Alitretinoin	300.4	Antineoplastic	39.89	45.76	69.94	82.22
Almotriptan	469.6	Antimigraine (esp. adolescent from 12 to 17 years of age)	15.12	7.35	-32.48	-1.18
Alosetron HCl	330.8	Antidiarrheal	14.64	13.32	79.09	84.48
Ambrisentan	378.4	Pulmonary hypertension treatment	-5.52	5.20	-25.71	-20.61
Amcinonide	502.6	Anti-inflammatory	31.24	39.97	55.43	55.86

Amikacin Disulfate	781.8	Antibiotic	9.17	14.56	13.78	8.06
Aminocaproic Acid	131.2	Hemostatic; Antifibrinolytic agent	14.29	10.95	-40.17	-1.16
Aminohippurate Na	217.2	Diagnostic Aid	8.97	6.57	-43.96	-9.87
Aminolevulinic Acid HCl	167.6	Antineoplastic	13.02	4.75	-39.56	-6.70
Amlexanox	298.3	Antihistaminic	58.83	62.04	44.46	60.50
Amphotericin B	924.1	Antifungal	20.80	17.25	-10.92	11.96
Arsenic Trioxide	197.8	Antineoplastic	-3.42	2.42	-27.78	-12.98
Artemether	298.4	Antimalarial	3.85	13.64	1.34	7.56
Articaine HCl	320.8	Anesthetic	5.28	-1.78	-25.48	-25.75
L-Ascorbic Acid	176.1	Antioxidant; Free Radical Scavenger; Vitamin	-22.32	-16.88	-29.88	-29.15
Asenapine Maleate	401.8	Antipsychotic	-1.99	-2.41	-12.79	-0.89
Atomoxetine HCl	291.8	Nootropic; Antidepressant	24.69	14.42	-31.83	13.96
Atorvastatin Calcium	1155.3	Antihyperlipidemic	21.39	6.53	-41.21	-13.04
Azacitidine	244.2	Antineoplastic	12.50	0.73	-41.99	-5.73
Azelaic Acid	188.2	Antineoplastic; Dermatologic	8.57	1.65	-34.84	-14.83
Azelastine HCl	418.4	Antihistaminic	24.13	24.82	-24.95	2.57
Bacitracin	1422.7	Antibiotic	-4.53	-3.01	-12.59	-4.00
Baclofen	213.7	Muscle relaxant	-6.56	-0.54	-28.36	-21.76
Balsalazide	357.3	Anti-inflammatory; Anti-Ulcer; Gastrointestinal Agent	-8.42	0.41	-30.18	-22.37
Beclomethasone Dipropionate	521	Anti-asthmatic; Anti-inflammatory	24.13	13.19	46.49	49.99
Benazepril HCl	461	Antihypertensive	-8.46	-20.71	-18.96	-21.84
Bendamustine HCl	394.7	Antineoplastic	13.41	6.66	-43.33	-11.95
Bendroflumethiazide	421.4	Diuretic; antihypertensive	8.05	-6.20	-30.74	-2.53
Benzotropine Mesylate	403.5	Antiparkinsonian	20.72	19.39	-4.17	38.23
Betaine	117.2	Homocystinuria	13.65	2.01	-39.89	-16.33
Bethanechol Chloride	196.7	Parasympathomimetic	6.31	0.41	-34.28	-12.31
Bimatoprost	415.6	Antihypertensive; Antiglaucomic	35.01	38.28	-19.01	5.89
Biperiden HCl	347.9	Antiparkinson treatment	-1.24	7.71	-25.18	-8.99
Bisoprolol Fumarate	767	Antihypertensive	-6.56	-0.50	-26.59	-15.04
Brimonidine	292.1	Glaucoma treatment	-9.29	-3.24	-21.31	-19.47
Bromfenac	334.2	Analgesic	-3.06	-4.06	-13.30	-13.60
Brompheniramine Maleate	435.3	Antiallergic	20.08	6.16	-32.96	-0.83
Budesonide	430.5	Anti-inflammatory; Bronchodilator	31.04	13.87	30.48	61.18
Bupropion	239.7	Antidepressant	9.32	1.33	-32.13	-3.03
Busulfan	246.3	Antineoplastic	10.75	3.20	-35.34	-9.78
Butorphanol-(+)-Tartrate (Schedule Iv)	477.6	Analgesics; Opioid; Antitussive	12.98	3.79	-28.57	-4.30
Capreomycin Disulfate	864.9	Antibiotic	6.66	8.26	-7.61	9.20
Carbinoxamine Maleate	406.9	Antihistamine; anticholinergic	0.27	11.32	-25.10	-18.32
Carglumic Acid	190.2	Hyperammonaemia treatment	-1.67	-7.66	-28.87	-18.73
Carmustine	214.1	Antineoplastic	-4.49	-5.97	-15.85	-21.58

Cefaclor	367.8	Antibiotic	25.92	21.31	6.98	36.23
Cefadroxil	381.4	Antibiotic	10.83	5.02	-36.71	-7.58
Cefazolin Na	476.5	Antibiotic	13.97	3.42	-33.52	-9.81
Cefdinir	395.4	Antibiotic	8.09	-6.25	-31.50	-10.08
Cefditoren Pivoxil	620.7	Antibiotic	74.04	75.87	81.47	86.35
Cefixime	453.5	Antibiotic	-3.86	4.25	-26.19	-11.25
Cefotetan Disodium	619.6	Antibiotic	-6.52	-8.16	-25.31	-19.03
Cefoxitin Na	449.4	Antibiotic	-10.49	-5.33	-22.85	-23.28
Cefpodoxime Proxetil	557.6	Antibiotic	6.19	18.39	52.25	60.47
Cefprozil	389.4	Antibiotic	1.07	-7.20	11.63	21.97
Ceftibuten	410.4	Antibiotic	15.40	8.12	-29.22	4.60
Ceftizoxim Na	405.4	Antibiotic	18.34	6.25	-24.72	2.07
Ceftriaxone Na	576.6	Antibiotic	14.88	12.59	-26.19	-1.95
Cefuroxime Axetil	510.5	Antibiotic	16.15	13.28	-13.68	10.88
Cefuroxime Na	446.4	Antibiotic	7.34	10.08	-24.50	-0.42
Cephalexin Monohydrate	365.4	Antibiotic	1.07	3.01	-19.49	-1.16
Chenodiol (Chenodeoxycholic Acid)	392.6	Cholagogue and Choleric	-6.04	0.82	-15.12	-6.32
Chlorhexidine Dihydrochloride	578.4	Anti-infective; disinfectant	73.36	70.94	80.23	75.20
Chlorothiazide	295.7	Diuretic; antihypertensive	-0.24	-5.24	-9.56	-15.39
Chlorpropamide	276.7	Hypoglycemic Agent	-13.46	-9.81	-47.68	-41.89
Chlorthalidone	338.8	Antihypertensive; Diuretic	-11.64	-15.33	-52.00	-43.21
Chlorzoxazone	169.6	Muscle relaxant	-13.23	-2.46	-42.37	-41.62
Ciclesonide	540.7	Inhibits rhinitis and treatment for allergy	63.71	66.33	82.13	82.86
Ciclopirox	207.3	Antifungal	28.82	34.22	18.53	13.93
Cidofovir	279.2	Antiviral	-9.93	-8.44	-41.96	-37.40
Cilostazol	369.5	Vasodilator; Platelet Aggregation Inhibitor	11.87	8.21	1.84	-2.65
Cinacalcet HCl	393.9	Calcimimetic	32.31	49.36	76.92	60.74
Cisatracurium Besylate	1243.5	Neuromuscular Blocking Agent	24.77	25.14	-24.47	-24.46
Cisplatin (Cis-Diamineplatinum(II) Dichloride)	300.1	Antineoplastic	59.94	61.86	68.55	70.92
Cladribine	285.7	Antineoplastic	-28.63	-21.94	-54.02	-53.77
Clavulanate Potassium	237.3	Antibiotic adjuvant	-29.03	-24.40	-59.89	-61.14
Clobazam	300.7	Anticonvulsant	-34.39	-28.51	-43.33	-54.48
Clofazimine	473.4	Antibacterial; Leprostatic Agents; Dye	-80.68	-85.17	77.50	80.63
Clomipramine HCl	351.3	Antidepressant	-21.88	-4.01	-4.86	0.93
Clonazepam	315.7	Anticonvulsant; Hypnotic and Sedative	-21.52	-13.73	-31.27	-37.37
Clotrimazole	344.8	Antifungal	97.98	98.18	89.05	89.64
Cloxacillin Na	475.9	Antibiotic	-49.00	-16.24	-36.91	-46.67
Colchicine	399.4	A natural product that is used as a medication used for gout	-19.42	-13.14	-37.24	-45.17

Colistimethate Na	1749.8	Antibiotic	-6.71	-12.31	-13.98	-23.08
Colistin Sulfate	1267.6	Antibiotic; Antibacterial	-7.98	-11.22	-0.56	-4.65
Cortisone Acetate	402.5	Anti-inflammatory; Corticosteroid	-44.75	-31.34	-43.61	-49.25
Cyclobenzaprine HCl	311.8	Muscle relaxant	-20.21	-20.89	-27.58	-33.55
Cyclopentolate	291.4	Mydriatic	-43.83	-23.95	-57.23	-66.83
Cycloserine	102.1	Antibiotic	-25.33	-26.91	-47.73	-60.82
Cysteamine HCl	113.6	Radiation-protective agent; Nephropathic cystinosis therapy.	-32.32	-25.41	-48.81	-62.78
Dactinomycin (= Actinomycin D)	1255.4	Antineoplastic	3.41	-0.32	-19.87	-27.54
Dalfampridine (4-Aminopyridine)	94.1	Multiple sclerosis and Lambert-Eaton myasthenic syndrome treatment	-20.21	-31.11	-37.89	-48.99
Dantrolene Na	336.2	Muscle relaxant	-23.79	-43.70	-20.73	-31.06
Dapsone	248.3	Antibacterial (against Mycobacterium leprae)	-14.89	-16.10	-21.01	-34.38
Daptomycin	1620.7	Antibiotic	-31.09	-22.12	-54.83	-53.45
Darifenacin HBr	507.5	Overactive bladder and urinary incontinence treatment	3.13	-0.91	-17.95	-30.12
Darunavir	547.7	Antiviral	86.03	83.90	-8.52	-8.46
Dasatinib	488	Antineoplastic	32.95	33.81	79.22	77.23
Decitabine	228.2	Treatment of myelodysplastic syndromes (MDS)	-28.39	-31.38	-51.57	-60.32
Deferasirox	373.4	Rationally designed iron chelator	-23.63	-27.82	-41.53	-50.31
Deferoxamine Mesylate	656.8	Iron chelator used in iron poisoning	-27.91	-26.82	-37.24	-49.90
Demeclocycline HCl	501.3	Antibiotic	-14.10	-20.12	-29.53	-48.29
Desipramine HCl	302.8	Antidepressant	-5.52	-21.76	-12.14	-8.70
Desogestrel	310.5	Contraceptive	63.67	68.25	91.20	92.22
Desonide	416.5	Anti-inflammatory; Corticosteroid	3.33	2.97	-13.90	-15.01
Desoximetasone	376.5	Anti-inflammatory; Glucocorticoid	-48.24	-40.92	32.30	26.58
Desvenlafaxine Succinate Hydrate	399.5	Antidepressant	-27.08	-26.78	-52.71	-64.10
Dexchlorpheniramine Maleate	390.9	Antihistamine; antiallergic	-30.57	-28.42	-50.48	-63.72
Dexmedetomidine HCl	236.7	Sedative	86.50	86.95	89.00	88.09
Dexrazoxane	268.3	Cardioprotective agent	-26.60	-20.94	-19.16	-30.12
Diatrizoate Meglumine	809.1	Radiocontrast agent	-21.52	-18.88	-43.43	-43.12
Diazepam	284.7	Anti-anxiety agent; Hypnotic and Sedative	-18.39	-26.23	-9.78	-11.90
Dicloxacillin Na Salt Monohydrate	510.3	Antibiotic	-1.63	-16.97	-24.83	-31.79
Dicyclomine HCl	345.9	Antispasmodic; Intestinal hypermotility treatment; relieves the symptoms of Irritable Bowel Syndrome (IBS)	-3.10	-4.83	-43.10	-37.75
Dienogest	311.4	Contraceptive	-61.26	-64.59	-36.12	-39.31
Diffmaprednate	508.6	Corticosteroid; Anti- inflammatory	16.55	2.38	23.96	28.13
Digoxin	780.9	Antiarrhythmic; Cardiotonic	-29.62	-29.28	-44.85	-62.61

Dimenhydrinate	470	Nausea and motion sickness treatment	-26.72	-22.72	-43.99	-53.68
Disopyramide	339.5	Antiarrhythmic	-20.53	-26.78	-40.45	-46.17
Dopamine HCl	189.6	Catecholamine neurotransmitter	-20.21	-32.34	-35.44	-45.29
Doripenem	420.5	Ultra-broad spectrum antibiotic	-10.25	-24.49	-31.40	-41.68
Doxapram HCl H2O	433	Respiratory stimulant	-13.86	-16.47	-29.25	-39.42
Doxepin HCl	315.8	Psychotropic Agent with Tricyclic Antidepressant and Anxiolytic Properties	-26.45	-25.09	-34.20	-40.45
Droperidol	379.4	Sedative/Anti-nausea/Anesthesia Adjunct	-12.87	-19.29	1.74	-7.52
Drospirenone	366.5	Contraceptive	-28.95	-43.06	-4.25	-2.89
Duloxetine HCl	333.9	Antidepressant	-4.29	-0.68	-1.27	-11.69
Dutasteride	528.5	Treatment of benign prostatic hyperplasia (BPH) and male pattern baldness (MPB).	-0.40	-3.46	-19.85	-33.29
Dyphylline	254.2	Antiasthmatic	-28.43	-24.81	-36.30	-51.72
Econazole Nitrate	444.7	Antifungal	97.30	97.76	97.12	97.24
Eflornithine HCl	218.6	Facial hirsutism and African trypanosomiasis (sleeping sickness) treatment	-23.55	-21.44	-32.79	-38.66
Epinastine HCl	285.8	Antiallergic; Antihistamine; Mast cell stabilizer	-20.81	-26.00	-19.29	-30.41
Epirubicin HCl	580	Antineoplastic	10.56	13.51	30.38	29.75
Eplerenone	414.5	Potassium-sparing diuretic; Antihypertensive	-20.09	-15.10	-29.12	-36.49
Eptifibatide	832	Antiplatelet; anticoagulant	-21.20	-12.77	-35.32	-45.50
Erythromycin	733.9	Macrolide antibiotic	-0.40	-3.05	-36.93	-46.11
Estramustine Phosphate Na	566.4	Antineoplastic	-25.93	-12.22	-20.63	-21.11
Estropipate	436.6	Hormonal replacement; Antineoplastic	-8.02	-12.68	-23.46	-29.18
Eszopiclone	388.8	Nonbenzodiazepine hypnotic	-24.62	-18.06	-28.97	-30.30
Ethambutol Dihydrochloride	277.2	Bacteriostatic; antimycobacterial	-14.50	-19.75	-25.61	-27.39
Ethinyl Estradiol	296.4	Contraceptive	53.71	58.12	85.01	84.27
Ethionamide	166.2	Antibiotic; antimycobacterial	-9.26	-10.72	-50.13	-42.89
Ethosuximide	141.2	Anticonvulsant	-21.28	-9.58	-49.85	-48.87
Etodolac	287.4	Nonsteroidal anti-inflammatory	-15.53	-9.85	-45.78	-48.11
Etomidate	244.3	General anaesthetic; sedative	77.21	80.43	-4.48	-7.20
Etonogestrel	324.5	Hormonal contraceptive	45.77	45.44	86.68	85.18
Everolimus	958.2	Immunosuppressant	79.12	81.71	73.41	73.65
Ezetimibe	409.4	Hypercholesterolemia	56.21	55.11	90.60	91.61
Febuxostat	316.4	Hyperuricemia and gout treatment	-10.96	4.06	-12.67	-18.85
Fexofenadine HCl	538.1	Antihistamine	-7.27	3.74	-23.69	-27.92
Fingolimod	307.5	Immunomodulator approved for treating multiple sclerosis.	59.03	65.69	67.11	63.90
Flavoxate HCl	427.9	Muscle relaxant	-18.62	-16.28	1.24	-0.74
Flucytosine	129.1	Antimycotic	-35.18	-19.07	-55.61	-59.99
Fludarabine Phosphate	365.2	Antineoplastic; immunosuppressant	-34.58	-23.13	-55.94	-59.47

Fludrocortisone Acetate	422.5	Hormonal replacement for aldosterone (in adrenal insufficiency and salt wasting)	-39.90	-26.05	-34.00	-46.61
Flunisolide	434.5	Anti-inflammatory	26.28	22.63	63.78	66.05
Fluocinonide	494.5	Anti-inflammatory	13.06	8.31	78.24	73.47
Fluorometholone	376.5	Anti-inflammatory	61.37	65.38	-7.79	-21.61
Flurandrenolide	436.5	Anti-inflammatory	-6.40	-13.41	-26.24	-33.79
Fluticasone Propionate	500.6	Anti-asthma and anti-allergy (rhinitis)	57.32	63.46	42.87	28.89
Fluvoxamine Maleate	434.4	Antidepressant	-13.98	-12.54	-34.18	-32.73
Fomepizole	82.1	Antidote in confirmed or suspected methanol or ethylene glycol poisoning	-27.52	-22.90	-44.62	-55.01
Formoterol	344.4	Antiasthmatic; Bronchodilator	-23.07	-28.74	-57.16	-61.90
Foscarnet Na (Sodium Phosphonoformate Tribasic Hexahydrate)	300	Antiviral	-33.15	-32.39	-51.52	-63.63
Fosfomycin Calcium	178.1	Broad-spectrum antibiotic; Anti-Bacterial	-25.37	-21.16	-47.65	-58.17
Fosphenytoin Na Pentahydrate	496.3	Antiepileptic	-24.22	-32.39	-44.39	-57.06
Gemifloxacin	389.4	Antibiotic	-30.18	-20.57	-33.90	-48.55
Glycopyrrolate Iodide	445.3	Adjuvant; Anesthetic	-10.80	-22.99	-39.46	-46.35
Griseofulvin	352.8	Antifungal	-8.38	-20.12	-19.90	-26.92
Guanidine HCl	95.5	Myasthenia treatment	-23.19	-17.83	-25.63	-29.30
Halcinonide	455	Anti-inflammatory	-17.51	-19.57	78.39	75.23
Halobetasol Propionate	485	Vasoconstrictor; Anti-inflammatory	-18.78	-32.75	-48.59	-57.21
Hexachlorophene	406.9	Antiseptic; bacteriostatic	98.69	98.45	94.87	96.10
Homatropine Methylbromide	370.3	Anti-Ulcer; Antispasmodic	-27.20	-29.83	-42.06	-52.86
Hydralazine HCl	196.6	Muscle relaxant	-24.86	-23.45	-5.01	-11.72
Hydrochlorothiazide	297.7	Antihypertensive; Diuretic	-19.06	-26.14	-44.26	-50.75
Hydroflumethiazide	331.3	Antihypertensive; Diuretic	-22.87	-29.74	-39.97	-49.75
Hydroxocobalamin HCl	1383.8	Anti-anemic; Hematinic	-16.48	-15.05	-26.87	-32.32
Hydroxychloroquine Sulfate	434	Antirheumatic Agent; Antimalarial	-12.35	-22.94	-29.32	-40.68
Hydroxyurea	76.1	Antineoplastic	-15.17	-23.26	-26.59	-25.54
Hydroxyzine Dihydrochloride	447.8	Antihistamine (1st Generation)/Antiemetic/Hypnotic/Mild Anxiolytic	-22.48	-13.50	-36.78	-48.26
Ibutilide Fumarate	500.7	Class III antiarrhythmic	-16.84	-18.15	-48.18	-49.37
Iloperidone	426.5	Antipsychotic	90.91	92.15	85.29	84.86
Indinavir	613.8	Antiviral; Anti-HIV Agent	91.94	90.24	40.04	41.28
Irbesartan	428.5	Antihypertensive	-8.90	-8.12	-24.83	-32.09
Irinotecan HCl	623.1	Antineoplastic; Colon cancer treatment.	-24.74	-15.64	-37.97	-50.96
Isocarboxazid	231.3	Antidepressant and anxiolytic	-10.21	-20.43	-36.60	-46.20
Isosorbide Dinitrate	236.1	Vasodilator used in the treatment of angina pectoris	-20.49	-22.53	-38.55	-37.98
Isotretinoin (13-Cis-Retinoic Acid)	300.4	Antineoplastic; Cystic acne treatment	43.15	43.43	90.29	91.46
Isradipine	371.4	Antihypertensive	71.61	75.82	80.54	75.97

Kanamycin Sulfate	582.6	Antibiotic	-31.01	-34.53	-50.63	-52.16
Ketorolac Tromethamine	376.4	Anti-inflammatory (NSAID)	-9.26	-9.81	17.97	17.71
Labetalol HCl	364.9	Antihypertensive	-27.48	-31.47	-50.13	-57.97
Lacosamide	250.3	Adjunctive treatment of partial-onset seizures and diabetic neuropathic pain	-30.14	-23.63	-46.97	-57.44
Lactulose	342.3	Gastrointestinal Agent	-26.76	-26.32	-46.39	-54.80
Lamivudine	229.3	Antiviral	-27.48	-33.16	-38.70	-49.52
Lansoprazole	369.4	Antiulcer	49.30	50.87	80.06	78.20
Lenalidomide	259.3	Multiple myeloma treatment	-17.43	-22.21	-34.84	-40.60
Leucovorin Calcium Pentahydrate	601.6	Helps eliminate methotexate toxicity without compromising the antitumor effect	-15.17	-23.03	-32.71	-36.99
Levalbuterol HCl	275.8	Bronchodilator; antiasthmatic	-15.05	-20.57	-21.56	-25.78
Levobunolol HCl	327.9	Glaucoma treatment	-30.42	-29.65	-51.34	-56.09
Levocarnitine	161.2	Gastric and pancreatic stimulant; hyperlipoproteinemia treatment	-28.19	-31.75	-49.47	-59.79
Levocetirizine Dihydrochloride	461.8	Antihistamine	-25.93	-28.65	-50.99	-67.21
Levothyroxine Na	798.9	Antithyroid Agent	15.56	10.18	88.70	86.41
Lindane	290.8	Scabicide and pediculicide	11.03	13.60	-32.31	-46.20
Liothyronine Na	673	Hormone Replacement Agent	-4.69	-8.89	93.28	93.95
Lopinavir	628.8	Antiviral; Anti-HIV Agent	81.30	77.65	81.80	77.96
Lorazepam	321.2	Anti-anxiety agent; Hypnotic and Sedative	-31.29	-23.67	-14.28	-18.47
Loteprednol Etabonate	467	Anti-inflammatory; Anti-Allergic	34.26	29.47	39.05	39.14
Loxapine Succinate	445.9	Antipsychotic	-13.11	-13.41	16.73	21.56
Mafenide HCl	222.7	Bacteriostatic sulfonamide; Adjuvant treatment for secondary and tertiary burns.	-12.51	-15.42	-27.93	-37.07
Malathion	330.4	Lice treatment	77.69	76.96	37.66	41.63
Mannitol	182.2	Osmotic diuretic; Sweetener	-15.61	-12.68	-34.94	-39.45
Maraviroc	513.7	Antiviral; Anti-HIV Agent	-8.30	-11.54	-36.43	-41.54
Mechlorethamine HCl	192.5	Antineoplastic; vesicant and necrotizing irritant destructive to mucous membranes	-18.62	-13.04	-25.15	-39.48
Meclizine Dihydrochloride	463.9	Antiemetic; Anti-Allergic	14.37	20.35	72.50	70.57
Meclofenamate Na	318.1	Non-steroidal anti-inflammatory agent with antipyretic and antigranulation activities.	-14.65	-15.05	-29.25	-24.37
Mefloquine HCl	414.8	Antimalarial	16.51	17.66	11.35	8.62
Mepenzolate Bromide	420.3	Antiulcer	-10.57	-6.16	-17.29	-23.46
Mepivacaine HCl	282.8	Anesthetic	-0.96	-2.60	-6.45	-12.72

Table S4: Primer sequences used for quantitative real-time PCR from murine tissue.

Gene	Forward	Reverse	Ref.
CYP2C29	5'GCCTCAAAGCCTACTGTCA-3'	5'- AACGCCAAAACCTTTAATC-3'	(1)
CYP2C37	5'-ATACTCTATATTTGGGCAGG-3'	5'- GTTCCTCCACAAGGCAAC-3'	(1)
CYP2C38	5'-TTGCCTTCTGTAATCCCC-3'	5'-TCTAACGCAGGAATGGATAAAC-3'	(2)
CYP2C39	5'-GGAGACAGAGCTGTGGC-3'	5'-TAAAAACAATGCCAAGGCCG-3'	(1)
CYP2C44	5'-CTTTCCAACGAGCGATTCCC-3'	5'-TGTTTCTCCTCCTCGATCTTGC-3'	(3)
CYP2J6	5'-GGAGACAACAATGATTAGTC-3'	5'-CTATCAGCAAGTCTTGCTGC-3'	(4)
CYP3A11	5'-GACAAACAAGCAGGGATGGAC-3'	5'- CCAAGCTGATTGCTAGGAGCA-3'	(5)

Supplementary methods:

Behavioural Tests

For the dynamic cold plate test, mice were put on a metal plate. The plate temperature changed gradually from 25°C to 0°C with a rate of 12°C/min. The time until jumping or nocifensive responses of the hind paw occurred was measured and the cut-off time was set to 200s. For the acetone test, a drop of acetone was applied on the mid plantar area of the hind paw and the time of nocifensive responses, such as shaking, flinching and licking was measured (6).

For the determination of mechanical or thermal hypersensitivity, mice were kept in test cages on an elevated grid for at least 2 h to allow accommodation. Baseline measurements were performed using a Dynamic Plantar Aesthesiometer or a Hargreaves

Apparatus (Ugo Basile, Comerio, VA, Italy) detecting withdrawal latency of the hind paws after mechanical stimulation. Paw withdrawal latencies (PWL) were determined in seconds (s) \pm 0.1 with a cut-off time of 20 s. The non-injected and injected paws were measured alternately in intervals of 5-10 min. For all behavioral tests the investigator was blinded for treatment or genotype of the mice.

Determination of lipidomic profiles by liquid chromatography-tandem mass spectrometry (LC-MS/MS)

Stock solutions with 2500 ng/ml of all analytes were prepared in methanol. Working standards were obtained by further dilution with a concentration range of 0.1-250 ng/ml for leukotrienes, HETEs, prostanoids, EETs, EpOMEs and DiHOMEs and HODEs. Sample extraction was performed with liquid-liquid-extraction. Therefore, tissue or cell culture medium was extracted twice with 600 μ l ethyl acetate. The combined organic phases were removed at a temperature of 45° C under a gentle stream of nitrogen. The residues were reconstituted with 50 μ l of methanol/water/ (50:50, v/v), centrifuged for 2 min at 10,000xg and then transferred to glass vials (Macherey-Nagel, Düren, Germany) prior to injection into the LC-MS/MS system.

To measure endocannabinoid/endovanilloid concentrations, the deuterated substances AEA-d8, PEA-d5, OEA-d2, 1-AG-d5 2-AG-d5, 1-OG-d5 and NADA-d8 were used as internal standards. 2 cycles of ethylacetate extraction were performed. 50 μ l ethylacetate were added to the tissue sample and the sample was homogenized using a swing mill (Retsch, Haan, Germany; 25 Hz for 2.5 minutes). After centrifugation (3 min, 20,238 g) the organic phase was removed and the extraction was repeated with 150 μ l of

ethylacetate. The two ethylacetate fractions were combined and evaporated at a temperature of 45 °C under a gentle stream of nitrogen and frozen at -80 °C till the day of measurement. The residues were reconstituted in 50 µl of acetonitrile and centrifuged for 3 min at 20,238 g. The residues were transferred in glass vials and 10 µl were injected into the LC-MS/MS system as described previously in more detail (7).

Instrumentation for lipid measurement

The LC-MS/MS system consisted of a QTrap 5500 (AB Sciex, Darmstadt, Germany) equipped with a Turbo-V source operating in negative electrospray ionization mode, an Agilent 1200 binary HPLC pump and degasser (Agilent, Waldbronn, Germany), and an HTC Pal autosampler (CTC analytics, Zwingen, Switzerland). High-purity nitrogen for the mass spectrometer was produced by a NGM 22-LC-MS nitrogen generator (cmc Instruments, Eschborn, Germany).

For the chromatographic separation of EETs, endocannabinoids and leukotrienes, Gemini NX C18 column and precolumn (150 x 2 mm inner diameter, 5 µm particle size, and 110 Å pore size; Phenomenex, Aschaffenburg, Germany) or a Luna C18-column (150 mm Lx2 mm ID, 5 µm particle size, Phenomenex, Aschaffenburg, Germany) were used. A linear gradient was used at a flow rate of 0.5 ml/min with a total run time of 17.5 min. Mobile phase A consist of water: ammonia (100:0.05, v/v), and mobile phase B of acetonitrile:ammonia (100:0.05, v/v). The gradient changed from 85% A to 10% within 12 min. These conditions were held for 1 min. Then, the mobile phase shifted back to 85% A within 0.5 min and it was maintained for 4 min to reequilibrate the column. For the chromatographic separation of prostanoids, a Synergi 4u Hydro-RP column (150 x 2 mm inner diameter, 4 µm, Phenomenex, Aschaffenburg, Germany) and a precolumn

of same material were used. Chromatographic separation was carried out in gradient elution mode at a flow rate of 0.3 ml/min. Total run time was 16 min. Mobile phase A consisted of water/formic acid (100:0.0025, v/v), and mobile phase B of acetonitrile/formic acid (100:0.0025, v/v). The linear gradient started with 90% A for 1 min and then changed to 60% A within 1 min. It was held for 1 min at 60% in phase A. Within 1min, the mobile phase shifted to 50% in phase A and was held for 2 min. Within 2 min, the mobile phase shifted to 10% A and was held for 1 min. Composition of the gradient shifted back to 90% A in one min and it was maintained for 6 min to re-equilibrate the column. A volume of 20 μ l (EETs, leukotrienes) or 45 μ l (prostanoids) of the extracted samples were injected into the LC-MS/MS system. Quantification was performed with Analyst software version 1.5 (Applied Biosystems) using the internal standard method (isotope-dilution mass spectrometry). Ratios of analyte peak area and internal standard area (y-axis) were plotted against concentration (x-axis), and calibration curves were calculated by least-squares regression with 1/square concentration weighting.

Calcium-imaging setup

Cells were illuminated by an UV light source (Xenon lamp, 75 watts, Nikon, NY, USA), 340 nm and 380 nm excitation alternated by a LEP MAC 5000 filter wheel (Spectra services, NY, USA), and fluorescence emission captured by Cool SNAP ES camera (Princeton Instruments, NJ, USA) or a Leica DFC360 FX.340/380 ratiometric images were processed, background corrected, and analyzed with IPLab software (Scientific Analytics, CA, USA).

Patch clamp recordings from spinal cord slices and DRG neurons

The slices were perfused with Krebs's solution (8-10 ml/min) that was saturated with 95% O₂ and 5% CO₂ at 26°C for at least 1-3h prior to experiment. The Krebs's solution contains (in mM): NaCl [11]7, KCl [3.6], CaCl₂ [2.5], MgCl₂ 1.2, NaH₂PO₄ [1.2], NaHCO₃ [25], and glucose [11]. The whole-cell patch-clamp recordings were made from lamina II neurons in voltage-clamp mode. Under a dissecting microscope with transmitted illumination, the substantia gelatinosa (lamina II) is clearly visible as a relatively translucent band across the dorsal horn. Patch pipettes were fabricated from thin-walled, borosilicate, glass-capillary tubing (1.5 mm outer diameter; World Precision Instruments).. The resistance of a typical patch pipette is 5–10 MΩ. The internal solution contained the following (in mM): [135] potassium gluconate, [5] KCl, [0.5] CaCl₂, [2] MgCl₂, [5] EGTA, [5] HEPES, and [5] ATP-Mg. Membrane currents were amplified with an Axopatch 200A amplifier (Molecular Devices) in voltage-clamp mode. Signals were filtered at 2 kHz and digitized at 5 kHz. Data were stored with a personal computer using pClamp 6 software and analyzed with Mini Analysis (Synaptosoft). Those cells that showed >5% changes from the baseline levels were regarded as responding ones.

Whole-cell patch clamp recordings were conducted in small-diameter (18-25 μm) neurons at room temperature (25 °C) using an Axopatch-200B amplifier (Axon Instruments). The patch pipettes were pulled from borosilicate capillaries (World Precision Instruments, Inc.). Pipette resistance was 4-6 MΩ for recording, and the internal solution contains (in mM): 126 K-gluconate, 10 NaCl, 1 MgCl₂, 10 EGTA, 2 NaATP, and 0.1 MgGTP, adjusted to pH 7.3 with KOH and osmolality 295-300 mOsm. The recordings were performed in an extracellular solution that contains (in mM): 140 NaCl, 5 KCl, 1 MgCl₂, 10 HEPES, 10 glucose, adjusted

to pH 7.4 with NaOH and osmolality 300-310 mOsm. To record the inward currents induced by telmisartan (10 μ M), capsaicin (200 nM), AITC (75 μ M) or GSK1016790A (1 μ M), voltage clamp was conducted at holding membrane potential of -60 mV. The inward currents were low-pass filtered at 1 kHz, and were digitized at a sampling rate of 5 kHz with Digidata 1322A (Axon Instruments). The pClamp10 (Axon Instruments) software was used during recordings and data analysis.

Supplementary references

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